

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



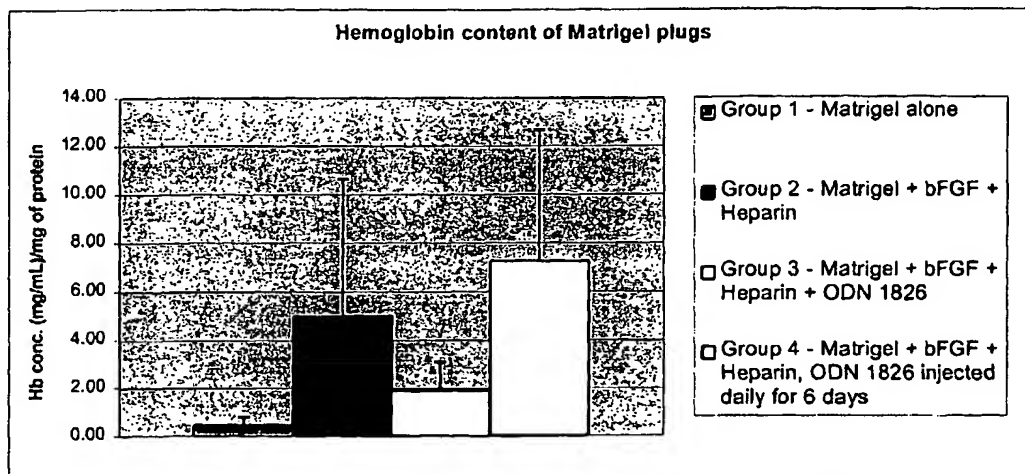
(43) International Publication Date  
11 July 2002 (11.07.2002)

PCT

(10) International Publication Number  
**WO 02/053141 A2**

- (51) International Patent Classification<sup>7</sup>: **A61K 31/00**
- (21) International Application Number: PCT/US01/48458
- (22) International Filing Date:  
14 December 2001 (14.12.2001)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
60/255,534 14 December 2000 (14.12.2000) US
- (71) Applicant: **COLEY PHARMACEUTICAL GROUP, INC.** [US/US]; Suite 101, 93 Worcester Street, Wellesley, MA 02481 (US).
- (72) Inventor: **BRATZLER, Robert, L.**; 84 Barns Hill Road, Concord, MA 01742 (US).
- (74) Agent: **TREVISAN, Maria, A.**; Wolf, Greenfield & Sacks, P.C., 600 Atlantic Avenue, Boston, MA 02210 (US).
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:**  
— without international search report and to be republished upon receipt of that report
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: INHIBITION OF ANGIOGENESIS BY NUCLEIC ACIDS



(57) Abstract: The invention relates to methods and products for inhibiting angiogenesis. At least one antiangiogenic nucleic acid molecule is administered to a subject to prevent or treat unwanted angiogenesis. Non-nucleic acid antiangiogenic agents also can be administered.

## **INHIBITION OF ANGIOGENESIS BY NUCLEIC ACIDS**

### **Background of the Invention**

Blood vessels are the means by which oxygen and nutrients are supplied to living  
5 tissues and waste products are removed from living tissue. Angiogenesis refers to the process  
by which new blood vessels are formed. See, for example, the review by Folkman and Shing,  
*J. Biol. Chem.* 267(16):10931-10934, 1992. Thus, where appropriate, angiogenesis is a  
critical biological process. It is essential in reproduction, development and wound repair.  
However, inappropriate angiogenesis can have severe negative consequences. For example, it  
10 is only after many solid tumors are vascularized as a result of angiogenesis that the tumors  
have a sufficient supply of oxygen and nutrients that permit it to grow rapidly and  
metastasize. Because maintaining the rate of angiogenesis in its proper equilibrium is so  
critical to a range of functions, it must be carefully regulated in order to maintain health. The  
angiogenesis process is believed to begin with the degradation of the basement membrane by  
15 proteases secreted from endothelial cells (EC) activated by mitogens such as vascular  
endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF). The cells  
migrate and proliferate, leading to the formation of solid endothelial cell sprouts into the  
stromal space, then, vascular loops are formed and capillary tubes develop with formation of  
tight junctions and deposition of new basement membrane.

20 In adults, the proliferation rate of endothelial cells is typically low compared to other  
cell types in the body. The turnover time of these cells can exceed one thousand days.  
Physiological exceptions in which angiogenesis results in rapid proliferation typically occurs  
under tight regulation, such as found in the female reproduction system and during wound  
healing.

25 The rate of angiogenesis involves a change in the local equilibrium between positive  
and negative regulators of the growth of microvessels. The therapeutic implications of  
angiogenic growth factors were first described by Folkman and colleagues over two decades  
ago (Folkman, *N. Engl. J. Med.* 285:1182-1186, 1971). Abnormal angiogenesis occurs when  
the body loses at least some control of angiogenesis, resulting in either excessive or  
30 insufficient blood vessel growth. For instance, conditions such as ulcers, strokes, and heart  
attacks may result from the absence of angiogenesis normally required for natural healing. In  
contrast, excessive blood vessel proliferation can result in tumor growth, tumor spread,  
blindness, psoriasis and rheumatoid arthritis.

- 2 -

There are instances where a greater degree of angiogenesis is desirable, e.g., increasing blood circulation, wound healing, and ulcer healing. For example, recent investigations have established the feasibility of using recombinant angiogenic growth factors, such as fibroblast growth factor (FGF) family (Yanagisawa-Miwa et al., *Science*, 257:1401-1403, 1992; Baffour et al., *J. Vasc. Surg.* 16:181-91, 1992), endothelial cell growth factor (ECGF; Pu et al., *J. Surg. Res.* 54:575-83, 1993), and more recently, vascular endothelial growth factor (VEGF) to expedite and/or augment collateral artery development in animal models of myocardial and hindlimb ischemia (Takeshita et al., *Circulation*, 90:228-234, 1994; Takeshita et al., *J. Clin. Invest.* 93:662-70, 1994).

Conversely, there are instances where inhibition of angiogenesis is desirable. For example, many diseases are driven by persistent unregulated angiogenesis, also sometimes referred to as "neovascularization". In arthritis, new capillary blood vessels invade the joint and destroy cartilage. In diabetes, new capillaries invade the vitreous of the eye, bleed, and cause blindness. Ocular neovascularization is the most common cause of blindness. Tumor growth and metastasis are angiogenesis-dependent. A tumor must continuously stimulate the growth of new capillary blood vessels for the tumor itself to grow.

The current approved treatment of these diseases is inadequate. Agents which prevent continued angiogenesis, such as drugs (e.g. TNP-470), monoclonal antibodies, antisense nucleic acids and proteins (e.g., angiostatin and endostatin) are currently being tested, but have not been approved. Although preliminary results with the antiangiogenic proteins are promising, they are relatively large in size and are difficult to use and produce. Moreover, proteins are subject to enzymatic degradation. Thus, new agents that inhibit angiogenesis are needed. New antiangiogenic agents that show improvement in size, ease of production, stability and/or potency would be desirable.

### **Summary of the Invention**

It has now been discovered that nucleic acid molecules, including oligonucleotides, have intrinsic antiangiogenesis properties apart from the proteins such nucleic acids may encode.

According to one aspect of the invention, methods for inhibiting angiogenesis are provided. The methods include administering to a subject in need of such treatment at least one antiangiogenic nucleic acid molecule in an amount effective to inhibit angiogenesis in the subject. In some embodiments, two or more antiangiogenic nucleic acid molecules are

- 3 -

administered. In other embodiments, non-nucleic acid antiangiogenic agents also are administered and agents that are effective against other aspects of an angiogenic condition (e.g., anticancer agents) can also be administered. In some embodiments, the angiogenesis is associated with a condition selected from the group consisting of rheumatoid arthritis, psoriasis, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, Osler-Webber Syndrome, myocardial angiogenesis, plaque neovascularization, telangiectasia, hemophiliac joints, angiofibroma, and wound granulation. In other embodiments, the angiogenesis is not associated with a cancer or tumor, but may be associated with an eye or ocular disorder such as those described herein. In still other embodiments, the angiogenesis is associated with embryo implantation. In certain embodiments, the angiogenesis is associated with conditions involving excessive or abnormal stimulation of endothelial cells such as but not limited to intestinal adhesions, atherosclerosis, scleroderma, and hypertrophic scars, i.e., keloids.

In other aspects of the invention, compositions are provided that include at least one antiangiogenic nucleic acid molecule, formulated in a pharmaceutically-acceptable carrier and in an effective amount for inhibiting angiogenesis. The compositions in certain embodiments include non-nucleic acid antiangiogenic agents and/or agents that are effective against other aspects of an angiogenic condition (e.g., anticancer agents).

According to still other aspects the invention, kits are provided that include a first container housing at least one antiangiogenic nucleic acid molecule and instructions for administering the antiangiogenic nucleic acid molecule to a subject having unwanted angiogenesis. In certain embodiments, a second container housing at least one non-nucleic acid antiangiogenic agent is also provided. In other embodiments of the foregoing kits, another container housing at least one anticancer agent is provided. In certain embodiments, the instructions relate to administering the antiangiogenic nucleic acid to a subject having a condition that is not cancer or a tumor, and examples of such conditions are listed throughout the specification.

A nucleic acid molecule is an element of each aspect of the invention. Preferred nucleic acid molecules include at least one sequence set forth as SEQ ID NOs: 1-1093. The nucleic acids useful according to the invention are synthetic or natural (isolated) nucleic acids. The nucleic acid may be administered alone or in conjunction with a pharmaceutically-acceptable carrier and optionally other therapeutic agents. In some embodiments the nucleic



- 4 -

acid is a CpG nucleic acid, including those having an unmethylated CpG motif, a T-rich nucleic acid, or a poly G nucleic acid.

The nucleic acid in some embodiments has a nucleotide backbone which includes at least one backbone modification, such as a phosphorothioate modification or other phosphate modification. In some embodiments the modified backbone is a peptide modified oligonucleotide backbone. The nucleotide backbone may be chimeric, or the nucleotide backbone is entirely modified.

The nucleic acid can have any length greater than 6 nucleotides, but in some embodiments is between 8 and 100 nucleotide residues in length. In other embodiments the nucleic acid comprises at least 20 nucleotides, at least 24 nucleotides, at least 27, nucleotides, or at least 30 nucleotides. The nucleic acid may be single stranded or double stranded. In some embodiments the nucleic acid is isolated and in other embodiments the nucleic acid may be a synthetic nucleic acid. The antiangiogenic nucleic acids in some instances are not antisense molecules.

The CpG nucleic acid in one embodiment contains at least one unmethylated CpG dinucleotide having a sequence including at least the following formula: 5' X<sub>1</sub> X<sub>2</sub>CGX<sub>3</sub> X<sub>4</sub> 3' wherein C is unmethylated, wherein X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub>, and X<sub>4</sub> are nucleotides. In one embodiment the 5' X<sub>1</sub> X<sub>2</sub>CGX<sub>3</sub> X<sub>4</sub> 3' sequence of the CpG nucleic acid is a non-palindromic sequence, and in other embodiments it is a palindromic sequence.

In some embodiments X<sub>1</sub>X<sub>2</sub> are nucleotides selected from the group consisting of: GpT, GpG, GpA, ApA, ApT, ApG, CpT, CpA, CpG, TpA, TpT, and TpG; and X<sub>3</sub>X<sub>4</sub> are nucleotides selected from the group consisting of: TpT, CpT, ApT, TpG, ApG, CpG, TpC, ApC, CpC, TpA, ApA, and CpA. In other embodiments X<sub>1</sub>X<sub>2</sub> are GpA or GpT and X<sub>3</sub>X<sub>4</sub> are TpT. In yet other embodiments X<sub>1</sub> or X<sub>2</sub> or both are purines and X<sub>3</sub> or X<sub>4</sub> or both are pyrimidines or X<sub>1</sub>X<sub>2</sub> are GpA and X<sub>3</sub> or X<sub>4</sub> or both are pyrimidines. In one embodiment X<sub>2</sub> is a T and X<sub>3</sub> is a pyrimidine.

In other embodiments the CpG nucleic acid has a sequence selected from the group consisting of SEQ ID NO: 1, 3, 4, 14-16, 18-24, 28, 29, 33-46, 49, 50, 52-56, 58, 64-67, 69, 71, 72, 76-87, 90, 91, 93, 94, 96, 98, 102-124, 126-128, 131-133, 136-141, 146-150, 152-153, 155-171, 173-178, 180-186, 188-198, 201, 203-214, 216-220, 223, 224, 227-240, 242-256, 258, 260-265, 270-273, 275, 277-281, 286-287, 292, 295-296, 300, 302, 305-307, 309-312, 314-317, 320-327, 329, 335, 337-341, 343-352, 354, 357, 361-365, 367-369, 373-376, 378-385, 388-392, 394, 395, 399, 401-404, 406-426, 429-433, 434-437, 439, 441-443, 445, 447,

448, 450, 453-456, 460-464, 466-469, 472-475, 477, 478, 480, 483-485, 488, 489, 492, 493, 495-502, 504-505, 507-509, 511, 513-529, 532-541, 543-555, 564-566, 568-576, 578, 580, 599, 601-605, 607-611, 613-615, 617, 619-622, 625-646, 648-650, 653-664, 666-697, 699-706, 708, 709, 711-716, 718-732, 736, 737, 739-744, 746, 747, 749-761, 763, 766-767, 769, 772-779, 781-783, 785-786, 7900792, 798-799, 804-808, 810, 815, 817, 818, 820-832, 835-846, 849-850, 855-859, 862, 865, 872, 874-877, 879-881, 883-885, 888-904, and 909-913.

In some embodiments the T rich nucleic acid is a poly T nucleic acid comprising 5' TTTT 3'. In yet other embodiments the poly T nucleic acid comprises 5' X<sub>1</sub> X<sub>2</sub>TTTTX<sub>3</sub> X<sub>4</sub> 3' wherein X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub> and X<sub>4</sub> are nucleotides. In some embodiments X<sub>1</sub>X<sub>2</sub> is TT and/or X<sub>3</sub>X<sub>4</sub> is TT. In other embodiments X<sub>1</sub>X<sub>2</sub> is selected from the group consisting of TA, TG, TC, AT, AA, AG, AC, CT, CC, CA, CG, GT, GG, GA, and GC; and/or X<sub>3</sub>X<sub>4</sub> is selected from the group consisting of TA, TG, TC, AT, AA, AG, AC, CT, CC, CA, CG, GT, GG, GA, and GC.

The T rich nucleic acid may have only a single poly T motif or it may have a plurality of poly T nucleic acid motifs. In some embodiments the T rich nucleic acid comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, or at least 8 T motifs. In other embodiments it comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, or at least 8 CpG motifs. In some embodiments the plurality of CpG motifs and poly T motifs are interspersed.

In yet other embodiments at least one of the plurality of poly T motifs comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, or at least 9 contiguous T nucleotide residues. In other embodiments the plurality of poly T motifs is at least 3 motifs and wherein at least 3 motifs each comprises at least 3 contiguous T nucleotide residues or the plurality of poly T motifs is at least 4 motifs and wherein the at least 4 motifs each comprises at least 3 contiguous T nucleotide residues.

The T rich nucleic acid may include one or more CpG motifs. The motifs may be methylated or unmethylated. In other embodiments the T rich nucleic acid is free of one or more CpG dinucleotides.

In other embodiments the T rich nucleic acid has poly A, poly G, and/or poly C motifs. In other embodiments the T rich nucleic acid is free of two poly C sequences of at least 3 contiguous C nucleotide residues. Preferably the T rich nucleic acid is free of two poly A sequences of at least 3 contiguous A nucleotide residues. In other embodiments the T rich nucleic acid comprises a nucleotide composition of greater than 25% C or greater than 25%

A. In yet other embodiments the T rich nucleic acid is free of poly-C sequences, poly G sequences or poly-A sequences.

In some cases the T rich nucleic acid may be free of poly T motifs, but rather, comprises a nucleotide composition of greater than 25% T. In other embodiments the T rich nucleic acid may have poly T motifs and also comprise a nucleotide composition of greater than 25% T. In some embodiments the T rich nucleic acid comprises a nucleotide composition of greater than 25% T, greater than 30% T, greater than 40% T, greater than 50% T, greater than 60% T, greater than 80% T, or greater than 90% T nucleotide residues. . The T rich nucleic acid in some embodiments is selected from the group consisting of SEQ ID NOs: 59-63, 73-75, 142, 215, 226, 241, 267-269, 282, 301, 304, 330, 342, 358, 370-372, 393, 433, 471, 479, 486, 491, 497, 503, 556-558, 567, 694, 793-794, 797, 833, 852, 861, 867, 868, 882, 886, 905, 907, 908, and 910-913. In other embodiments the T rich nucleic acids are sequence selected from the group consisting of SEQ ID NOs: 64, 98, 112, 146, 185, 204, 208, 214, 224, 233, 244, 246, 247, 258, 262, 263, 265, 270-273, 300, 305, 316, 317, 343, 344, 350, 352, 354, 374, 376, 392, 407, 411-413, 429-432, 434, 435, 443, 474, 475, 498-501, 518, 687, 692, 693, 804, 862, 883, 884, 888, 890, and 891.

In some embodiments the poly G nucleic acid comprises: 5' X<sub>1</sub>X<sub>2</sub>GGGX<sub>3</sub>X<sub>4</sub> 3' wherein X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub>, and X<sub>4</sub> are nucleotides. In embodiments at least one of X<sub>3</sub> and X<sub>4</sub> are a G or both of X<sub>3</sub> and X<sub>4</sub> are a G. In other embodiments the poly G nucleic acid comprises the following formula: 5' GGGNGGG 3' wherein N represents between 0 and 20 nucleotides. In yet other embodiments the poly G nucleic acid comprises the following formula: 5' GGGNGGGNGGG 3' wherein N represents between 0 and 20 nucleotides. The poly G nucleic acid in some embodiments is selected from the group consisting of SEQ ID NOs. : 5, 6, 73, 215, 267-269, 276, 282, 288, 297-299, 355, 359, 386, 387, 444, 476, 531, 557-559, 733, 768, 795, 796, 914-925, 928-931, 933-936, and 938. In other embodiments the poly G nucleic acid includes a sequence selected from the group consisting of SEQ ID NOs; 67, 80-82, 141, 147, 148, 173, 178, 183, 185, 214, 224, 264, 265, 315, 329, 434, 435, 475, 519, 521-524, 526, 527, 535, 554, 565, 609, 628, 660, 661, 662, 725, 767, 825, 856, 857, 876, 892, 909, 926, 927, 932, and 937.

The poly G nucleic acid may include one or more CpG motifs or T-rich motifs. The CpG motifs may be methylated or unmethylated. In other embodiments the poly G nucleic acid is free of one or more CpG dinucleotides or poly-T motifs.

- 7 -

The nucleic acid molecules and optionally other agents may be administered by any route known in the art for delivering medicaments. The medicaments may be administered separately or together, in the same pharmaceutical formulation or separate formulations, by the same route or by different routes. In one embodiment the nucleic acid molecule(s) is administered on a routine schedule. In another embodiment the other agent(s) (e.g., antiangiogenesis agents, anticancer agents) is administered on a routine schedule.

Each of the limitations of the invention can encompass various embodiments of the invention. It is, therefore, anticipated that each of the limitations of the invention involving any one element or combinations of elements can be included in each aspect of the invention.

#### **Brief Description of the Drawings**

Figure 1 is a histogram showing the effect of a CpG nucleic acid on angiogenesis as measured by hemoglobin content.

The drawing is not required for enablement of the claimed invention.

#### **Detailed Description of the Invention**

The present invention includes compositions that include antiangiogenic nucleic acids and methods of using the antiangiogenic nucleic acids for the treatment of diseases that are mediated by angiogenesis. The invention includes antiangiogenic nucleic acids having various nucleotide sequences. The present invention comprises a method of treating undesired angiogenesis in a human or animal comprising the steps of the administering to the human or animal with the undesired angiogenesis a composition comprising an effective amount of, for example, an antiangiogenic nucleic acid.

As used herein, the term "angiogenesis" means the generation of new blood vessels into a tissue or organ. Under normal physiological conditions, humans or animals undergo angiogenesis only in very specific restricted situations. For example, angiogenesis is normally observed in wound healing, fetal and embryonal development and formation of the corpus luteum, endometrium and placenta. The term "endothelium" means a thin layer of flat epithelial cells that lines serous cavities, lymph vessels, and blood vessels. The term "endothelial inhibiting activity" means the capability of a molecule to inhibit angiogenesis in general and, for example, to inhibit the growth of bovine capillary endothelial cells in culture in the presence of fibroblast growth factor.

- 8 -

Antiangiogenic nucleic acids are effective in treating diseases or processes that are mediated by, or involve, angiogenesis. The present invention includes the method of treating an angiogenesis mediated disease with an effective amount of antiangiogenic nucleic acids. The angiogenesis mediated diseases include, but are not limited to, solid tumors; blood born  
5 tumors such as leukemias; tumor metastasis; benign tumors, for example hemangiomas, acoustic neuromas, neurofibromas, trachomas, and pyogenic granulomas; pre-malignant tumors; rheumatoid arthritis; psoriasis; ocular angiogenic diseases, for example, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis; Osler-Webber Syndrome; myocardial  
10 angiogenesis; plaque neovascularization; telangiectasia; hemophiliac joints; angiofibroma; and wound granulation.

Antiangiogenic nucleic acids may be useful in the treatment of disease of excessive or abnormal stimulation of endothelial cells. These diseases include, but are not limited to, intestinal adhesions, atherosclerosis, scleroderma, and hypertrophic scars, i.e., keloids.  
15 Antiangiogenic nucleic acid can be used as a birth control agent by preventing vascularization required for embryo implantation.

Antiangiogenic nucleic acids may be useful in the treatment of conditions characterized by abnormal epithelial cell proliferation, such as proliferative dermatologic disorders. These include conditions such as keloids, seborrheic keratosis, papilloma virus  
20 infection (e.g. producing verruca vulgaris, verruca plantaris, verruca plana, condylomata, etc.) and eczema.

Antiangiogenic nucleic acids may be useful in the treatment of precancerous lesions such as epithelial precancerous lesions. An epithelial precancerous lesion is a lesion of epithelial cell origin that has a propensity to develop into a cancerous condition. An example  
25 is a precancerous skin lesion. Epithelial precancerous skin lesions also arise from other proliferative skin disorders such as hemangiomas, keloids, eczema and papilloma virus infections producing verruca vulgaris, verruca plantaris and verruca planar. The symptoms of the epithelial precancerous lesions include skin-colored or red-brown macule or papule with dry adherent scales. Actinic keratosis is the most common epithelial precancerous lesion  
30 among fair skinned individuals. It is usually present as lesions on the skin which may or may not be visually detectable. The size and shape of the lesions varies. It is a photosensitive disorder and may be aggravated by exposure to sunlight. Bowenoid actinic keratosis is another form of an epithelial precancerous lesion. In some cases, the lesions may develop

- 9 -

into an invasive form of squamous cell carcinoma and may pose a significant threat of metastasis. Other types of epithelial precancerous lesions include hypertrophic actinic keratosis, arsenical keratosis, hydrocarbon keratosis, thermal keratosis, radiation keratosis, viral keratosis, Bowen's disease, erythroplakia of queyrat, oral erythroplakia, leukoplakia, and intraepidermal epithelialoma.

Antiangiogenic nucleic acids may be used in combination with other compositions and procedures for the treatment of diseases. For example, a tumor may be treated conventionally with surgery, radiation or chemotherapy combined with antiangiogenic nucleic acids and then antiangiogenic nucleic acids may be subsequently administered to the patient to extend the dormancy of micrometastases and to stabilize any residual primary tumor. In some instances it may be preferable to administer the antiangiogenic nucleic acids specifically to a site likely to harbor a metastatic lesion (that may or may not be clinically discernible at the time). A sustained release formulation implanted specifically at the site (or the tissue) where the metastatic lesion is likely to be would be suitable in these latter instances.

In some embodiments, the antiangiogenic nucleic acids of the invention do not interfere with specific receptor-ligand interactions at the cell surface of a cell, thereby causing the stimulation or inhibition of signaling through such receptors. These interactions include those involving heparin binding receptor, VEGF receptor, or EGF receptor.

In still other embodiments, the antiangiogenic nucleic acids are not antisense nucleic acids, meaning that they do not function by binding to complementary genomic DNA or RNA species within a cell and thereby inhibiting the function of said genomic DNA or RNA species. In important embodiments, the antiangiogenesis nucleic acid does not comprise a nucleic acid sequence that corresponds to a VEGF encoding sequence (or is complementary to a VEGF encoding sequence).

The effective dosage for inhibition of angiogenesis *in vivo*, which can be defined as inhibition of capillary endothelial cell proliferation and/or migration and/or blood vessel ingrowth, can be extrapolated from *in vitro* inhibition assays. *In vitro* assays have been developed to screen for inhibition of angiogenesis. Events that can be tested to assess angiogenesis inhibitors include proteolytic degradation of extracellular matrix and/or basement membrane, proliferation of endothelial cells, migration of endothelial cells, and capillary tube formation. The chick chorioallantoic membrane assay (CAM), described by Taylor and Folkman (*Nature* 297:307-312, 1982), can be used to determine whether the compound is capable of inhibiting neovascularization *in vivo*.

- 10 -

In some embodiments, the antiangiogenic nucleic acids are administered in doses, routes and schedules (and also in therapeutic cocktails) that would not result in the stimulation of an immune response.

The effective dosage is dependent not only on the sequence of the nucleic acid molecules used for inhibition of angiogenesis, but also on the method and means of delivery, which can be localized or systemic. For example, in some applications, as in the treatment of psoriasis or diabetic retinopathy, the inhibitor preferably is delivered in a topical or ophthalmic carrier. In other applications, as in the treatment of solid tumors, the inhibitor preferably is delivered by means of a biodegradable, polymeric implant.

An "antiangiogenic nucleic acid" as used herein is any nucleic acid containing an antiangiogenic motif or backbone that inhibits capillary endothelial cell proliferation and/or migration and/or blood vessel ingrowth.

The compounds useful according to the invention are nucleic acids. The nucleic acids may be double-stranded or single-stranded. Generally, double-stranded molecules may be more stable *in vivo*, while single-stranded molecules may have increased activity. The terms "nucleic acid" and "oligonucleotide" refer to multiple nucleotides (i.e. molecules comprising a sugar (e.g. ribose or deoxyribose) linked to a phosphate group and to an exchangeable organic base, which is either a substituted pyrimidine (e.g. cytosine (C), thymine (T) or uracil (U)) or a substituted purine (e.g. adenine (A) or guanine (G)) or a modified base. As used herein, the terms refer to oligoribonucleotides as well as oligodeoxyribonucleotides. The terms shall also include polynucleosides (i.e. a polynucleotide minus the phosphate) and any other organic base containing polymer. Nucleic acid molecules as used herein include vectors, e.g., plasmids, as well as oligonucleotides.

The terms "nucleic acid" and "oligonucleotide" also encompass nucleic acids or oligonucleotides with a covalently modified base and/or sugar. For example, they include nucleic acids having backbone sugars which are covalently attached to low molecular weight organic groups other than a hydroxyl group at the 3' position and other than a phosphate group at the 5' position. Thus modified nucleic acids may include a 2'-O-alkylated ribose group. In addition, modified nucleic acids may include sugars such as arabinose instead of ribose. Thus the nucleic acids may be heterogeneous in backbone composition thereby containing any possible combination of polymer units linked together such as peptide- nucleic acids (which have amino acid backbone with nucleic acid bases). In some embodiments the nucleic acids are homogeneous in backbone composition.

The substituted purines and pyrimidines of the nucleic acids include standard purines and pyrimidines such as cytosine as well as base analogs such as C-5 propyne substituted bases (Wagner et al., *Nature Biotechnology* 14:840- 844, 1996). Purines and pyrimidines include but are not limited to adenine, cytosine, guanine, thymine, 5-methylcytosine, 2-aminopurine, 2-amino-6-chloropurine, 2,6-diaminopurine, hypoxanthine, and other naturally and non-naturally occurring nucleobases, substituted and unsubstituted aromatic moieties.

The nucleic acid is a linked polymer of bases or nucleotides. As used herein with respect to linked units of a nucleic acid, "linked" or "linkage" means two entities are bound to one another by any physicochemical means. Any linkage known to those of ordinary skill in the art, covalent or non-covalent, is embraced. Such linkages are well known to those of ordinary skill in the art. Natural linkages, which are those ordinarily found in nature connecting the individual units of a nucleic acid, are most common. The individual units of a nucleic acid may be linked, however, by synthetic or modified linkages.

Whenever a nucleic acid is represented by a sequence of letters it will be understood that the nucleotides are in 5'→ 3' order from left to right and that "A" denotes adenosine, "C" denotes cytosine, "G" denotes guanosine, "T" denotes thymidine, and "U" denotes uracil unless otherwise noted.

Nucleic acid molecules useful according to the invention can be obtained from natural nucleic acid sources (e.g. genomic nuclear or mitochondrial DNA or cDNA), or are synthetic (e.g. produced by oligonucleotide synthesis). Nucleic acids isolated from existing nucleic acid sources are referred to herein as native, natural, or isolated nucleic acids. The nucleic acids useful according to the invention may be isolated from any source, including eukaryotic sources, prokaryotic sources, nuclear DNA, mitochondrial DNA, etc. Thus, the term nucleic acid encompasses both synthetic and isolated nucleic acids.

The term "isolated" as used herein refers to a nucleic acid which is substantially free of or which is separated from components which it is normally associated with in nature e.g., nucleic acids, proteins, lipids, carbohydrates or *in vivo* systems to an extent practical and appropriate for its intended use. In particular, the nucleic acids are sufficiently pure and are sufficiently free from other biological constituents of host cells so as to be useful in, for example, producing pharmaceutical preparations. Because an isolated nucleic acid of the invention may be admixed with a pharmaceutically-acceptable carrier in a pharmaceutical preparation, the nucleic acid may comprise only a small percentage by weight of the



- 12 -

preparation. The nucleic acid is nonetheless substantially pure in that it has been substantially separated from the substances with which it may be associated in living systems. The nucleic acids can be produced on a large scale in plasmids, (see Sambrook, T., *et al.*, "Molecular Cloning: A Laboratory Manual", Cold Spring Harbor laboratory Press, New York, 1989) and  
5 separated into smaller pieces or administered whole. After being administered to a subject the plasmid can be degraded into oligonucleotides. One skilled in the art can purify viral, bacterial, eukaryotic, etc. nucleic acids using standard techniques, such as those employing restriction enzymes, exonucleases or endonucleases.

For use in the instant invention, the nucleic acids can be synthesized *de novo* using  
10 any of a number of procedures well known in the art. For example, the b-cyanoethyl phosphoramidite method (Beaucage, S.L., and Caruthers, M.H., *Tet. Let.* 22:1859, 1981); nucleoside H-phosphonate method (Garegg *et al.*, *Tet. Let.* 27:4051-4054, 1986; Froehler *et al.*, *Nucl. Acid. Res.* 14:5399-5407, 1986, ; Garegg *et al.*, *Tet. Let.* 27:4055-4058, 1986, Gaffney *et al.*, *Tet. Let.* 29:2619-2622, 1988). These chemistries can be performed by a  
15 variety of automated oligonucleotide synthesizers available in the market.

In some embodiments, the nucleic acids useful according to the invention may function as immunostimulatory nucleic acids. An immunostimulatory nucleic acid is any nucleic acid, as described herein, which is capable of modulating an immune response. A nucleic acid which modulates an immune response is one which produces any form of  
20 immune stimulation, including, but not limited to, induction of a cytokine, B cell activation, T cell activation, monocyte activation. Immunostimulatory nucleic acids include, but are not limited to, CpG nucleic acids, T-rich nucleic acids, poly G nucleic acids, and nucleic acids having phosphate modified backbones, such as phosphorothioate backbones.

A "CpG nucleic acid" or a "CpG antiangiogenic nucleic acid" as used herein is a  
25 nucleic acid containing at least one unmethylated CpG dinucleotide (cytosine-guanine dinucleotide sequence, i.e. "CpG DNA" or DNA containing a 5' cytosine followed by 3' guanosine and linked by a phosphate bond) and inhibits angiogenesis. The entire CpG nucleic acid can be unmethylated or portions may be unmethylated but at least the C of the 5' CG 3' must be unmethylated.

30 In one embodiment the invention provides a CpG nucleic acid represented by at least the formula:



- 13 -

wherein  $X_1$  and  $X_2$  are nucleotides and  $N$  is any nucleotide and  $N_1$  and  $N_2$  are nucleic acid sequences composed of from about 0-25  $N$ 's each. In some embodiments  $X_1$  is adenine, guanine, or thymine and/or  $X_2$  is cytosine, adenine, or thymine. In other embodiments  $X_1$  is cytosine and/or  $X_2$  is guanine.

5 In other embodiments the CpG nucleic acid is represented by at least the formula:



wherein  $X_1$ ,  $X_2$ ,  $X_3$ , and  $X_4$  are nucleotides. In some embodiments,  $X_1X_2$  are nucleotides selected from the group consisting of: GpT, GpG, GpA, ApA, ApT, ApG, CpT, CpA, CpG, TpA, TpT, and TpG; and  $X_3X_4$  are nucleotides selected from the group consisting of: TpT, CpT, ApT, TpG, ApG, CpG, TpC, ApC, CpC, TpA, ApA, and CpA;  $N$  is any nucleotide and  $N_1$  and  $N_2$  are nucleic acid sequences composed of from about 0-25  $N$ 's each. In some  
10 embodiments,  $X_1X_2$  are GpA or GpT and  $X_3X_4$  are TpT. In other embodiments  $X_1$  or  $X_2$  or both are purines and  $X_3$  or  $X_4$  or both are pyrimidines or  $X_1X_2$  are GpA and  $X_3$  or  $X_4$  or both are pyrimidines.

15 In another embodiment the CpG nucleic acid has the sequence



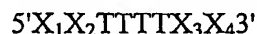
Examples of CpG nucleic acids according to the invention include but are not limited to those listed in Table 1, such as SEQ ID NOs: 1, 3, 4, 14-16, 18-24, 28, 29, 33-46, 49, 50, 52-56, 58, 64-67, 69, 71, 72, 76-87, 90, 91, 93, 94, 96, 98, 102-124, 126-128, 131-133, 136-  
20 141, 146-150, 152-153, 155-171, 173-178, 180-186, 188-198, 201, 203-214, 216-220, 223, 224, 227-240, 242-256, 258, 260-265, 270-273, 275, 277-281, 286-287, 292, 295-296, 300, 302, 305-307, 309-312, 314-317, 320-327, 329, 335, 337-341, 343-352, 354, 357, 361-365, 367-369, 373-376, 378-385, 388-392, 394, 395, 399, 401-404, 406-426, 429-433, 434-437, 439, 441-443, 445, 447, 448, 450, 453-456, 460-464, 466-469, 472-475, 477, 478, 480, 483-  
25 485, 488, 489, 492, 493, 495-502, 504-505, 507-509, 511, 513-529, 532-541, 543-555, 564-566, 568-576, 578, 580, 599, 601-605, 607-611, 613-615, 617, 619-622, 625-646, 648-650, 653-664, 666-697, 699-706, 708, 709, 711-716, 718-732, 736, 737, 739-744, 746, 747, 749-761, 763, 766-767, 769, 772-779, 781-783, 785-786, 7900792, 798-799, 804-808, 810, 815, 817, 818, 820-832, 835-846, 849-850, 855-859, 862, 865, 872, 874-877, 879-881, 883-885,  
30 888-904, and 909-913.

A "T rich nucleic acid" or "T rich antiangiogenic nucleic acid" is a nucleic acid which includes at least one poly T sequence and/or which has a nucleotide composition of greater than 25% T nucleotide residues and which inhibits angiogenesis. A nucleic acid having a

- 14 -

poly-T sequence includes at least four Ts in a row, such as 5'-TTTT-3'. Preferably the T rich nucleic acid includes more than one poly T sequence. In preferred embodiments the T rich nucleic acid may have 2, 3, 4, etc poly T sequences, such as SEQ ID NO:246 or SEQ ID NO:433. Other T rich nucleic acids have a nucleotide composition of greater than 25% T nucleotide residues, but do not necessarily include a poly T sequence. In these T rich nucleic acids the T nucleotide residues may be separated from one another by other types of nucleotide residues, i.e., G, C, and A. In some embodiments the T rich nucleic acids have a nucleotide composition of greater than 30%, 40%, 50%, 60%, 70%, 80%, 90%, and 99%, T nucleotide residues and every integer % in between. Preferably the T rich nucleic acids have at least one poly T sequence and a nucleotide composition of greater than 25% T nucleotide residues.

In one embodiment the T rich nucleic acid is represented by at least the formula:



wherein  $X_1$ ,  $X_2$ ,  $X_3$ , and  $X_4$  are nucleotides. In one embodiment  $X_1X_2$  is TT and/or  $X_3X_4$  is TT. In another embodiment  $X_1X_2$  are any one of the following nucleotides TA, TG, TC, AT, AA, AG, AC, CT, CC, CA, CG, GT, GG, GA, and GC; and  $X_3X_4$  are any one of the following nucleotides TA, TG, TC, AT, AA, AG, AC, CT, CC, CA, CG, GT, GG, GA, and GC.

In some embodiments it is preferred that the T-rich nucleic acid does not contain poly C (CCCC), poly A (AAAA), poly G (GGGG), CpG motifs, or multiple GGs. In other embodiments the T-rich nucleic acid includes these motifs. Thus in some embodiments of the invention the T rich nucleic acids include CpG dinucleotides and in other embodiments the T rich nucleic acids are free of CpG dinucleotides. The CpG dinucleotides may be methylated or unmethylated.

Examples of T rich nucleic acids that are free of CpG nucleic acids include but are not limited to those listed in Table 1, such as SEQ ID Nos: 59-63, 73-75, 142, 215, 226, 241, 267-269, 282, 301, 304, 330, 342, 358, 370-372, 393, 433, 471, 479, 486, 491, 497, 503, 556-558, 567, 694, 793-794, 797, 833, 852, 861, 867, 868, 882, 886, 905, 907, 908, and 910-913.

Examples of T rich nucleic acids that include CpG nucleic acids include but are not limited to those listed in Table 1, such as SEQ ID Nos: 64, 98, 112, 146, 185, 204, 208, 214, 224, 233, 244, 246, 247, 258, 262, 263, 265, 270-273, 300, 305, 316, 317, 343, 344, 350, 352, 354, 374, 376, 392, 407, 411-413, 429-432, 434, 435, 443, 474, 475, 498-501, 518, 687, 692, 693, 804, 862, 883, 884, 888, 890, and 891.

- 15 -

Poly G containing nucleic acids are also useful in accordance with the invention. A “poly G nucleic acid” or “poly G antiangiogenic nucleic acid” is a nucleic acid which includes at least one poly G sequence and/or which has a nucleotide composition of greater than 25% G nucleotide residues and which inhibits angiogenesis. A variety of references, including

5 Pisetsky and Reich, 1993 *Mol. Biol. Reports*, 18:217-221; Krieger and Herz, 1994, *Ann. Rev. Biochem.*, 63:601-637; Macaya et al., 1993, *PNAS*, 90:3745-3749; Wyatt et al., 1994, *PNAS*, 91:1356-1360; Rando and Hogan, 1998, In *Applied Antisense Oligonucleotide Technology*, ed. Krieg and Stein, p. 335-352; and Kimura et al., 1994, *J. Biochem.* 116, 991-994 describe the properties of poly G nucleic acids.

10 Poly G nucleic acids preferably are nucleic acids having the following formulas:



wherein  $X_1$ ,  $X_2$ ,  $X_3$ , and  $X_4$  are nucleotides. In preferred embodiments at least one of  $X_3$  and  $X_4$  are a G. In other embodiments both of  $X_3$  and  $X_4$  are a G. In yet other embodiments the preferred formula is 5' GGGN GGG 3', or 5' GGGN GGGN GGG 3' wherein N represents

15 between 0 and 20 nucleotides. In other embodiments the Poly G nucleic acid is free of unmethylated CG dinucleotides, such as, for example, the nucleic acids listed below as SEQ ID Nos: 5, 6, 73, 215, 267-269, 276, 282, 288, 297-299, 355, 359, 386, 387, 444, 476, 531, 557-559, 733, 768, 795, 796, 914-925, 928-931, 933-936, and 938. In other embodiments the poly G nucleic acid includes at least one unmethylated CG dinucleotide, such as, for example,

20 the nucleic acids listed above as SEQ ID Nos; 67, 80-82, 141, 147, 148, 173, 178, 183, 185, 214, 224, 264, 265, 315, 329, 434, 435, 475, 519, 521-524, 526, 527, 535, 554, 565, 609, 628, 660, 661, 662, 725, 767, 825, 856, 857, 876, 892, 909, 926, 927, 932, and 937.

The antiangiogenic nucleic acids of the invention can also be those which do not possess CpG, poly-G, or T-rich motifs.

25 Nucleic acids having modified backbones, such as phosphorothioate backbones, also fall within the class of immunostimulatory nucleic acids. U.S. Patents Nos. 5,723,335 and 5,663,153 issued to Hutcherson, et al. and related PCT publication WO95/26204 describe immune stimulation using phosphorothioate oligonucleotide analogues. These patents describe the ability of the phosphorothioate backbone to stimulate an immune response in a

30 non-sequence specific manner.

The antiangiogenic nucleic acid molecules may be any size of at least 6 nucleotides but in some embodiments are in the range of between 6 and 100 or in some embodiments between 8 and 35 nucleotides in size. Nucleic acids can be produced on a large scale in

- 16 -

plasmids. These may be administered in plasmid form or alternatively they can be degraded into oligonucleotides before administration.

“Palindromic sequence” shall mean an inverted repeat (i.e. a sequence such as ABCDEE'D'C'B'A' in which A and A' are bases capable of forming the usual Watson-Crick base pairs and which includes at least 6 nucleotides in the palindrome. *In vivo*, such sequences may form double-stranded structures. In one embodiment the nucleic acid contains a palindromic sequence. In some embodiments when the nucleic acid is a CpG nucleic acid, a palindromic sequence used in this context refers to a palindrome in which the CpG is part of the palindrome, and optionally is the center of the palindrome. In another embodiment the nucleic acid is free of a palindrome. A nucleic acid that is free of a palindrome does not have any regions of 6 nucleotides or greater in length which are palindromic. A nucleic acid that is free of a palindrome can include a region of less than 6 nucleotides which are palindromic.

A “stabilized nucleic acid molecule” shall mean a nucleic acid molecule that is relatively resistant to *in vivo* degradation (e.g. via an exo- or endo-nuclease). Stabilization can be a function of length or secondary structure. Nucleic acids that are tens to hundreds of kbs long are relatively resistant to *in vivo* degradation. For shorter nucleic acids, secondary structure can stabilize and increase their effect. For example, if the 3' end of an oligonucleotide has self-complementarity to an upstream region, so that it can fold back and form a sort of stem loop structure, then the oligonucleotide becomes stabilized and therefore exhibits more activity.

Some stabilized oligonucleotides of the instant invention have a modified backbone. It has been demonstrated that modification of the oligonucleotide backbone provides enhanced activity of the nucleic acids when administered *in vivo*. Nucleic acids, including at least two phosphorothioate linkages at the 5' end of the oligonucleotide and multiple phosphorothioate linkages at the 3' end, preferably 5, may provide maximal activity and protect the oligonucleotide from degradation by intracellular exo- and endo-nucleases. Other modified oligonucleotides include phosphodiester modified oligonucleotide, combinations of phosphodiester and phosphorothioate oligonucleotide, methylphosphonate, methylphosphorothioate, phosphorodithioate, and combinations thereof. Each of these combinations and their particular effects on immune cells is discussed in more detail in PCT Published Patent Applications claiming priority to U.S. Patent Nos. 6,207,646B1 and 6,239,116B1, the entire contents of which are hereby incorporated by reference. It is believed that these modified oligonucleotides may show more antiangiogenic activity due to enhanced

- 17 -

nuclease resistance, increased cellular uptake, increased protein binding, and/or altered intracellular localization.

Other stabilized oligonucleotides include: nonionic DNA analogs, such as alkyl- and aryl-phosphates (in which the charged phosphonate oxygen is replaced by an alkyl or aryl group), phosphodiester and alkylphosphotriesters, in which the charged oxygen moiety is alkylated. Oligonucleotides which contain diol, such as tetraethyleneglycol or hexaethyleneglycol, at either or both termini have also been shown to be substantially resistant to nuclease degradation.

For use *in vivo*, nucleic acids are preferably relatively resistant to degradation (*e.g.*, via endo- and exo-nucleases). Secondary structures, such as stem loops, can stabilize nucleic acids against degradation. Alternatively, nucleic acid stabilization can be accomplished via phosphate backbone modifications. One type of stabilized nucleic acid has at least a partial phosphorothioate modified backbone. Phosphorothioates may be synthesized using automated techniques employing either phosphoramidate or H-phosphonate chemistries. Aryl- and alkyl-phosphonates can be made, *e.g.*, as described in U.S. Patent No. 4,469,863; and alkylphosphotriesters (in which the charged oxygen moiety is alkylated as described in U.S. Patent No. 5,023,243 and European Patent No. 092,574) can be prepared by automated solid phase synthesis using commercially available reagents. Methods for making other DNA backbone modifications and substitutions have been described (Uhlmann, E. and Peyman, A., *Chem. Rev.* 90:544, 1990; Goodchild, J., *Bioconjugate Chem.* 1:165, 1990).

Other sources of nucleic acids useful according to the invention include standard viral and bacterial vectors, many of which are commercially available. In its broadest sense, a "vector" is any nucleic acid material which is ordinarily used to deliver and facilitate the transfer of nucleic acids to cells. The vector as used herein may be an empty vector or a vector carrying a gene which can be expressed. In the case when the vector is carrying a gene the vector generally transports the gene to the target cells with reduced degradation relative to the extent of degradation that would result in the absence of the vector. In this case the vector optionally includes gene expression sequences to enhance expression of the gene in target cells such as immune cells, but it is not required that the gene be expressed in the cell.

In general, vectors include, but are not limited to, plasmids, phagemids, viruses, other vehicles derived from viral or bacterial sources. Viral vectors are one type of vector and include, but are not limited to, nucleic acid sequences from the following viruses: retrovirus, such as Moloney murine leukemia virus, Harvey murine sarcoma virus, murine mammary

- 18 -

tumor virus, and Rous sarcoma virus; adenovirus, adeno-associated virus; SV40-type viruses; polyoma viruses; Epstein-Barr viruses; papilloma viruses; herpes virus; vaccinia virus; polio virus; and RNA virus such as a retrovirus. One can readily employ other vectors not named but known to the art. Some viral vectors are based on non-cytopathic eukaryotic viruses in which non-essential genes have been replaced with a nucleic acid to be delivered.

Non-cytopathic viruses include retroviruses, the life cycle of which involves reverse transcription of genomic viral RNA into DNA.

Standard protocols for producing empty vectors or vectors carrying genes (including the steps of incorporation of exogenous genetic material into a plasmid, transfection of a packaging cell line with plasmid, production of recombinant retroviruses by the packaging cell line, collection of viral particles from tissue culture media, and/or infection of the target cells with viral particles) are provided in Kriegler, M., "Gene Transfer and Expression, A Laboratory Manual," W.H. Freeman C.O., New York (1990) and Murry, E.J. Ed. "Methods in Molecular Biology," vol. 7, Humana Press, Inc., Clifton, New Jersey (1991).

Other vectors include plasmid vectors. Plasmid vectors have been extensively described in the art and are well-known to those of skill in the art. See e.g., Sambrook et al., "Molecular Cloning: A Laboratory Manual," Second Edition, Cold Spring Harbor Laboratory Press, 1989. In the last few years, plasmid vectors have been found to be particularly advantageous for delivering genes to cells *in vivo* because of their inability to replicate within and integrate into a host genome. Some plasmids, however, having a promoter compatible with the host cell, can express a peptide from a gene operatively encoded within the plasmid. Some commonly used plasmids include pBR322, pUC18, pUC19, pcDNA3.1, SV40, and pBlueScript. Other plasmids are well-known to those of ordinary skill in the art.

Additionally, plasmids may be custom designed using restriction enzymes and ligation reactions to remove and add specific fragments of DNA.

Exemplary antiangiogenic nucleic acid sequences include but are not limited to those antiangiogenic sequences shown in Table 1 (SEQ ID NO: 1 to SEQ ID NO:1093). The Table lists the SEQ ID NO, nucleotide sequence of the oligonucleotide (ODN sequence), and backbone modification, if any.

Backbone modifications are abbreviated as follows:

S = phosphorothioate

O = phosphodiester

SOS = phosphorothioate and phosphodiester chimeric with phosphodiester in middle

- 19 -

SO = phosphorothioate and phosphodiester chimeric with phosphodiester on 3' end

OS = phosphorothioate and phosphodiester chimeric with phosphodiester on 5' end

S2 = phosphorodithioate

S2O = phosphorodithioate and phosphodiester chimeric with phosphodiester on 3' end

5 OS2 = phosphorodithioate and phosphodiester chimeric with phosphodiester on 5' end

X = unknown

p-ethoxy = p-ethoxy backbone; see, e.g., US patent 6,015,886

PO = phosphodiester

ODN sequence symbols, other than a, c, g and t, are as follows:

10 i = inosine

n = a, c, g, or t

d = a, g or t

h = a, c or t

b = c, g or t; if "b" is single and is listed on 5' or 3' end of oligonucleotide, then "b"

15 indicates a biotin moiety attached to that end of the oligonucleotide

q = 5-methyl-cytosine

m = a or c

s = c or g

x = if "x" is single and is listed on 5' or 3' end of oligonucleotide, then "x" indicates a

20 biotin moiety attached to that end of the oligonucleotide

z = 5-methyl-cytidine

f = FITC moiety attached to 5' or 3' end of oligonucleotide

**Table 1**

SEQ ID NO:	ODN SEQUENCE	BACKBONE
1	tctcccagcgtgcgccat	S
2	ataatccagcttgaaccaag	S
3	ataatcgacgttcaagcaag	S
4	taccgcgtgcgaccctct	S
5	ggggagggt	S
6	ggggagggg	S
7	ggtgagggtg	S
8	tccatgtzgttcctgatgct	O
9	gctaccttagzgtga	O
10	tccatgazgttcctgatgct	O
11	tccatgacgttcztgatgct	O
12	gctagazgttagtgt	O
13	agctccatggtgctcactg	S
14	ccacgtcgaccctcaggcga	S
15	gcacatcgtcccgcagccga	S
16	gtcactcgtggtacctcga	S



- 20 -

17	gttgatacaggccagactttgttg	o
18	gattcaacttgcgtcatcttaggc	o
19	accatggacgaactgtttcccctc	s
20	accatggacgagctgtttcccctc	s
21	accatggacgacctgtttcccctc	s
22	accatggacgtactgtttcccctc	s
23	accatggacggtctgtttcccctc	s
24	accatggacgttctgtttcccctc	s
25	ccactcacatctgctgctccacaag	o
26	acttctcatagtccctttggtccag	o
27	tccatgagcttcctgagtct	o
28	gaggaaggigiggaigacgt	o
29	gtgaaticggttcicgggict	o
30	aaaaaa	s
31	cccccc	s
32	ctgtca	s
33	tcgtag	s
34	tcgtgg	s
35	cgtcgt	s
36	tccatgtoggtcctgagtct	sos
37	tccatgccggtcctgagtct	sos
38	tccatgacggtcctgagtct	sos
39	tccatgacggtcctgagtct	sos
40	tccatgtogatcctgagtct	sos
41	tccatgtogctcctgagtct	sos
42	tccatgtogttcctgagtct	sos
43	tccatgacgttcctgagtct	sos
44	tccataacgttcctgagtct	sos
45	tccatgacgtccctgagtct	sos
46	tccatcacgtgcctgagtct	sos
47	tccatgctggtcctgagtct	sos
48	tccatgtzggctcctgagtct	sos
49	ccgcttccctccagatgagctcatgggtttctccaccaag	o
50	cttgggtggagaaacccatgagctcatctggaggaagcgg	o
51	cccaaagggatgagaagtt	o
52	agatagcaaatacggtgacg	o
53	ggttcacgtgctcatggctg	o
54	tctcccagcgtgcgcat	s
55	tctcccagcgtgcgcat	s
56	taccgogtgcgacctct	s
57	ataatccagcttgaaccaag	s
58	ataatcgacgttcaagcaag	s
59	tccatgattttcctgatttt	o
60	ttgtttttttgtttttttgtttt	s
61	ttttttttgtttttttgtttt	o
62	tgctgcttttgtgcttttgtgctt	s
63	tgctgcttgtgcttttgtgctt	o
64	gcattcatcaggcgggcaagaat	o
65	taccgagottcgacgagatttca	o
66	gcatgacgttgagct	s
67	cacgttgaggggcat	s
68	ctgctgagactggag	s
69	tccatgacgttcctgacgtt	s
70	gcatgagcttgagctga	o
71	tcagcgtgcgcc	s
72	atgacgttcctgacgtt	s
73	ttttggggttttggggtttt	s

74	tctaggcttttttaggcttcc	S
75	tgcatttttttaggccacat	S
76	tctcccagcgtgcgtgcgcat	s
77	tctcccagcgggcat	s
78	tctcccagcgcgcat	s
79	tctcccagcgcgcat	s
80	ggggtgacgttcaggggg	sos
81	ggggtccagcgtgcgcatgggg	sos
82	ggggtgctgttcaggggg	sos
83	tccatgtcgttcctgtcgtt	s
84	tccatagcgttcctagcgtt	s
85	tcgtcgtgtctcgcgttctt	s
86	gcatgacgttgagct	Sos
87	tctcccagcgtgcgcatat	Sos
88	tccatgazgttcctgazgtt	S
89	gcatgazgttgagct	O
90	tccagcgtgcgcatata	sos
91	tctcccagcgtgcgcat	O
92	tccatgagcttcctgagct	O
93	gcatgtcgttgagct	sos
94	tctgacgttcctgacgtt	s
95	gcatgatgttgagct	o
96	gcatttcgaggagct	o
97	gcatgtagctgagct	o
98	tccaggacgttcctagttct	o
99	tccaggagcttcctagttct	o
100	tccaggatgttcctagttct	o
101	tccagtctaggcctagttct	o
102	tccagttcgagcctagttct	o
103	gcatggcgttgagct	sos
104	gcatagcgttgagct	sos
105	gcattgcgttgagct	sos
106	gcttgcggtgcgttt	sos
107	tctcccagcgttcgcatat	sos
108	tctcccagcgtgcgttatat	sos
109	tctccctgcgtgcgcatat	sos
110	tctgcgtgcgtgcgcatat	sos
111	tctcctagcgtgcgcatat	sos
112	tctcccagcgtgcgcctttt	sos
113	gctandeghhagc	o
114	tctgacgttccc	o
115	ggaagacgttaga	o
116	tctgacgttaga	o
117	tcagaccagctggcgggtgttctga	o
118	tcaggaacacccgaccagctggtctga	o
119	gctagtcgatagc	o
120	gctagtcgctagc	o
121	gcttgacgtctagc	o
122	gcttgacgttttagc	o
123	gcttgacgtcaagc	o
124	gctagacgttttagc	o
125	tccatgacattcctgatgct	o
126	gctagacgtctagc	o
127	ggctatgtcgttcctagcc	o
128	ggctatgtcgatcctagcc	o
129	ctcatgggtttctccaccaag	o
130	cttggtggagaaacccatgag	o

131	tccatgacgttcctagttct	o
132	ccgcttcctccagatgagctcatg	o
133	catgagctcatctggaggaagcgg	o
134	ccagatgagctcatgggtttctcc	o
135	ggagaaacccatgagctcatctgg	o
136	agcatcaggaacgacatgga	o
137	tccatgacgttcctgacgtt	RNA
138	gcgcgcgcgcgcgcgcgcgcg	o
139	ccggccggccggccggccgg	o
140	ttccaatcagcccccaccogctctggccccaccctcaccctcca	o
141	tggagggtgaggggtggggccagagcgggtggggctgattggaa	o
142	tcaaattgtgggattttcccatgagctct	o
143	agactcatgggaaaaatcccacatttga	o
144	tgccaagtgctgagtcactaataaaga	o
145	tctttattagtgactcagcacttggca	o
146	tgcaggaagtcggggttttccccaacccccc	o
147	ggggggttggggaaaaacccggacttcctgca	o
148	ggggacttttcgctggggactttccaggggactttcc	Sos
149	tccatgacgttcctctccatgacgttcctctccatgacgttcctc	o
150	gaggaacgtcatggagaggaacgtcatggagaggaacgtcatgga	o
151	ataatagagcttcaagcaag	s
152	tccatgacgttcctgacgtt	s
153	tccatgacgttcctgacgtt	sos
154	tccaggactttcctcaggtt	s
155	tcttgcatgctaaaggacgtcacattgcacaatottaataaggt	o
156	accttattaagattgtgcaatgtgacgtccttttagcatcgcaaga	o
157	tctgacgttcctggcggtcctgtcgct	o
158	tctgtcgctcctgtcgct	o
159	tctgacgttgaagt	o
160	tctgtcggttgaagt	o
161	tctggcggttgaagt	o
162	tctgocgttgaagt	o
163	tcttacgttgaagt	o
164	tctaacgttgaagt	o
165	tctcacgttgaagt	o
166	tctgacgatgaagt	o
167	tctgacgtgaagt	o
168	tctgacggtgaagt	o
169	tctgacgtagaagt	o
170	tctgacgtcgaagt	o
171	tctgacgtggaagt	o
172	tctgagcttgaagt	o
173	gggggacgttggggg	o
174	tctgacgttccttc	o
175	tctcccagcgagcgagcccat	s
176	tctgacgttcccctggcggtcccctgtcgct	0
177	tctgtcgctcctgtcgctcctgtcgct	0
178	tctggcggggaagt	o
179	tctgazgttgaagt	o
180	tcztgacgttgaagt	o
181	tctagcgttgaagt	o
182	tcagacgttgaagt	o
183	tctgacggggaagt	o
184	tctggcggtgaagt	o
185	ggctccggggagggaatttttgtctat	o
186	atagacaaaaattccctcccoggagcc	o
187	tccatgacgttccttgagtct	RNA

- 23 -

188	tcgtcgtgtctccgcttctt	so
189	tcgtcgtgtctccgcttctt	s20
190	tcgagacattgcacaatcatctg	o
191	cagattgtgcaatgtctcga	o
192	tccatgtcgttctctgatgcg	o
193	gcgatgtcgttctctgatgct	o
194	gcgatgtcgttctctgatgcg	o
195	tccatgtcgttccgcgcgcg	o
196	tccatgtcgttctctgccgct	o
197	tccatgtcgttctctgtagct	o
198	gcggcggcgccgcgcgcgc	o
199	atcaggaaacgtcatgggaagc	o
200	tccatgagcttctctgagtct	p-ethoxy
201	tcaacgctt	p-ethoxy
202	tcaagctt	p-ethoxy
203	tcctgtcgttctctgtcgtt	s
204	tccatgtcgtttttgtcgtt	s
205	tcctgtcgttctctgtcgtt	s
206	tcctgtcgttctctgtcgtt	s
207	btccattccatgacgttctctgatgcttcca	os
208	tcctgtcgtttttgtcgtt	s
209	tcgtcgtgtctccgcttctt	s
210	tcgtcgtgtctccgcttctt	s
211	tcgtcgtgttgcgttctt	s
212	tcctgtcgttctctgtcgttggaaacgacagg	o
213	tcctgtcgttctctgtcgtttcaacgtcaggaaacgacagga	o
214	ggggtctgtcgttttgggggg	sos
215	ggggtctgtcgttttgggggg	sos
216	tccggccgttgaagt	o
217	tccggacggtgaagt	o
218	tcccgccgttgaagt	o
219	tccagacggtgaagt	o
220	tcccgacggtgaagt	o
221	tccagagcttgaagt	o
222	tccatgtzgttctctgtzgtt	s
223	tccatgacgttctctgacgtt	sos
224	ggggttgacgttttgggggg	sos
225	tccaggacttctctcaggtt	s
226	tttttttttttttttttttt	s
227	tccatgccgttctctgccgtt	s
228	tccatggcgggcctggcggg	s
229	tccatgacgttctctgccgtt	s
230	tccatgacgttctctggcggg	s
231	tccatgacgttctctgccgtt	s
232	tccatgacggtctctgacggt	s
233	tccatgcgtgcgtgcgtttt	s
234	tccatgcgttgcgttgcgtt	s
235	Btccattccattcttaggcctgagtcttccat	os
236	tccatagcgttctctagcgtt	o
237	tccatgtcgttctctgtcgtt	o
238	tccatagcgatctctagcgat	o
239	tccattgcgttctctgcgtt	o
240	tccatagcgttctctagcgtt	o
241	tccatgattttctctgcagttctctgatttt	
242	tccatgacgttctctgcagttctctgacgtt	s
243	ggcggcgccggcgccggcg	o
244	tccacgacgttttgcacgtt	s

245	tcgtcggttgctggttgctgt	S
246	tcgtcggttttgctggttttgctgt	S
247	tcgtcggttgctggttttgctgt	S
248	gcgtgcgttgctggttgctgt	S
249	czggczggczggczggczgg	O
250	gcggcgggcgggcgcgcgccc	S
251	agicccgigaacgiattcac	O
252	tgctggttgctggttgctgt	S
253	tgctggttgctggttgctgt	S
254	tgctggttgctggttgctgt	S
255	tcgtcggtcgctgt	S
256	tgctggttgctgt	S
257	cccccccccccccccccc	S
258	tctagcggttttagcggtcc	SOS
259	tgcatccccaggccaccat	S
260	tcgtcggtcggtcggtcggt	SOS
261	tcgtcggttgctggttgctgt	SOS
262	tcgtcggttttgctggttttgctgt	SOS
263	tcgtcggttgctggttttgctgt	SOS
264	ggggagggaacttcttaaaattccccagaatgtt	O
265	aaacattctgggggaattttaagaagttcctccctccc	O
266	atgtttacttcttaaaattccccagaatgtt	O
267	aaacattctgggggaattttaagaagtaaacat	O
268	atgtttactagacaaaattccccagaatgtt	O
269	aaacattctgggggaattttgtctagtaaacat	O
270	aaaattgacgttttaaaaa	SOS
271	ccccttgacgttttcccccc	SOS
272	ttttcggttggttttgctgt	
273	tcgtcggttttgctggttttgctgt	SOS
274	ctgcagcctgggac	O
275	accggtcgtaattatagtaaaacc	O
276	ggtacctgtggggacattgtg	O
277	agcaccgaacgtgagagg	O
278	tccatgccgttcctgccgt	O
279	tccatgacggtcctgacgg	O
280	tccatgccgttcctgccgt	O
281	tccatgcgcgttcctgcgcgt	O
282	ctggtctttctgggtttttctgg	S
283	tcagggtgggggaacctt	SOS
284	tccatgazgttcctagttct	O
285	tccatgatgttcctagttct	O
286	cccgaagtcatttctcttaacctgg	O
287	ccaggttaagaggaaatgacttcggg	O
288	tctggzggggaagt	O
289	gzggzgggzggzggzggccc	X
290	tccatgtgcttcctgatgct	O
291	tccatgtccttcctgatgct	
292	tccatgtcggttcctagttct	
293	tccaagtagttcctagttct	O
294	tccatgtagttcctagttct	O
295	tcccgcggttcgcgcgt	S
296	tctggcggttcctggcggt	S
297	tctggagggggaagt	O
298	tctgggggggaagt	O
299	tctgggtggggaagt	O
300	tcgtcggttttgctggttttgctgt	O
301	ctggtctttctgggtttttctgg	O

302	tccatgacgttcctgacgtt	o
303	tccaggacttctctcagggtt	sos
304	tzgtzgttttztzgttttztzgtt	o
305	btcgtcgttttgcgttttgcgtttttt	os
306	gctatgacgttccaagg	s
307	tcaacgtt	s
308	tccaggactttcctcagggtt	o
309	ctctctgtaggcccgttgg	s
310	ctttccgttggaccctggg	s
311	gtccggggccaggccaaagtc	s
312	gtgcgcgcgagcccgaatc	s
313	tccatgaigtctcctgaigt	s
314	aatagtcgccataacaaaac	o
315	aatagtcgccatggcggggc	o
316	btttttccatgtcgttcctgatgctttt	os
317	tcctgtcgttgaagttttt	o
318	gctagcttttagagcttttagagctt	o
319	tgtgtttcccccccccc	o
320	tcgacgttcccccccccc	o
321	tcgtcgttcccccccccc	o
322	tcgtcgttcccccccccc	o
323	tcgccgttcccccccccc	o
324	tcgtcgatcccccccccc	o
325	tcctgacgttgaagt	s
326	tcctgccgttgaagt	s
327	tcctgacggtgaagt	s
328	tcctgagcttgaagt	s
329	tcctggcggggaagt	s
330	aaaatctgtgcttttaaaaaa	sos
331	gatccagtcacagtgcctggcagaatctggat	o
332	gatccagattctgccaggtcactgtgactggat	o
333	gatccagtcacagtgcactcagcagaatctggat	o
334	gatccagattctgctgagtcactgtgactggat	o
335	tcgtcgttccccccczzccc	o
336	tzgtggttcccccccccc	o
337	tzgtcgttcccccccccc	o
338	tcgtzgttcccccccccc	o
339	tcgtcgttcccccccccc	o
340	tcgtcgttcccccccccc	o
341	tcggcgttcccccccccc	o
342	ggccttttcccccccccc	o
343	tcgtcgttttgacgttttgcgtt	s
344	tcgtcgttttgacgttttgacgtt	s
345	ccgtcgttcccccccccc	o
346	gcgtcgttcccccccccc	o
347	tcgtcattcccccccccc	o
348	acgtcgttcccccccccc	o
349	ctgtcgttcccccccccc	o
350	btttttgcgtcgttcccccccccc	os
351	tcgtcgttccccccccccb	o
352	tcgtcgttttgcgttttgcgttb	o
353	tccagttccttcctcagtt	o
354	tzgtcgttttgcgttttgcgtt	o
355	tcctggaggggaagt	s
356	tcctgaaaaggaagt	s
357	tcgtcgttcccccccc	s
358	tzgtzgttttztzgttttztzgtt	s

- 26 -

359	ggggtcaagcttgagggggg	sos
360	tgctgcttccccccccccc	s
361	tcgtcgtcgtcgtt	s2
362	tcgtcgtcgtcgtt	s20
363	tcgtcgtcgtcgtt	os2
364	tcaacgttga	s
365	tcaacgtt	s
366	atagttttccatttttttac	
367	aatagtcgccatcgcgcgac	o
368	aatagtcgccatcccgggac	o
369	aatagtcgccatccccccc	o
370	tgctgcttttgtgcttttgcgtt	o
371	ctgtgctttctgtgttttctgtg	s
372	ctaattctttctaattttttctaa	s
373	tcgtcgttggtgtcgttggtgtcgtt	s
374	tcgtcgttggttgctggttttggtt	s
375	accatggacgagctgtttccctc	
376	tcgtcgttttgcgtgcgtt	s
377	ctgtaagtgaagcttgagag	
378	gagaacgctggaccttcc	
379	cgggcgactcagtcctatcgg	
380	gttctcagataaagcgggaaccagcaacagacacagaa	
381	ttctgtgtctgttgctgggtccgctttatctgagaac	
382	cagacacagaagcccgatagacg	
383	agacagacacgaaacgaccg	
384	gtctgtcccatgatctcgaa	
385	gctggccagcttacctccc	
386	ggggcctctatacaacctggg	
387	ggggtccctgagactgcc	
388	gagaacgctggaccttccat	
389	tccatgtcggctcctgatgct	
390	ctcttgcgacctggaaggta	
391	aggtacagccaggactacga	
392	accatggacgacctgtttccctc	
393	accatggattacctttttccctt	
394	atggaaggctccagcgttctc	o
395	agcatcaggaccgacatgga	o
396	ctctccaagctcacttacag	
397	tccctgagactgccccacctt	
398	gccacaaaacttgtccatg	
399	gtccatggcgtgcgggatga	
400	cctctatacaacctgggac	
401	cgggcgactcagtcctatcgg	
402	gcgctaccggtagcctgagt	
403	cgactgccgaacaggatatcggtgatcagcactgg	
404	ccagtgctgatcaccgatatcctgttcggcagtcg	
405	ccagggtgtatagaggc	
406	tctcccagcgtacgccat	s
407	tctcccagcgtgcgtttt	s
408	tctcccagcgtgcgccat	s
409	tctcccgctcgtgcgccat	s
410	ataatcgtcgttcaagcaag	s
411	tcgtcgttttgcgttttgcgt	s2
412	tcgtcgttttgcgttttgcgtt	s2
413	tcgtcgttttgcgttttgcgtt	s2
414	tcntcgtntntcgtntntcgtnt	s
415	tctcccagcgtcgccat	s

- 27 -

416	tctcccatcgctcgcoat	S
417	ataatcgctgcgttcaagaaag	S
418	ataatcgacgttcccccccc	S
419	tctatcgacgttcaagcaag	S
420	tcc tga cgg gg agt	S
421	tccatgacgttcctgatcc	
422	tccatgacgttcctgatcc	
423	tccatgacgttcctgatcc	
424	tcc tgg cgt gga agt	S
425	tccatgacgttcctgatcc	
426	tcgtcgctgttgctgtttctt	S
427	agcagctttagagctttagagctt	S
428	cccccccccccccccccccc	S
429	tcgtcgttttgtcgttttgtcgttttgtcgtt	S
430	tcgtcgttttttgtcgttttttgtcgtt	S
431	tcgtcgttttttttttttttt	S
432	tttttcaacgttgatttttt	SOS
433	tttttttttttttttttttttt	S
434	ggggtcgctcgttttggggg	
435	tcgtcgttttgtcgttttggggg	
436	tcgtcgctgtctccgcttcttcttgcc	S
437	tcgtcgctgtctccg	S
438	ctgtaagtgaagcttgagag	
439	gagaacgctggaccttccat	
440	ccaggttgatagaggc	
441	gctagacgttagcgtga	
442	ggagctcttcgaacgccata	
443	tctccatgatggttttatcg	
444	aagggtgggcagctctcagga	
445	atcggaggactggcgcccg	
446	ttaggacaaggcttaggggtg	
447	accacaacgagaggaacgca	
448	ggcagtcaggctcaccggg	
449	gaaccttccatgctgtt	
450	gctagacgttagcgtga	
451	gcttgaggggcctgtaagtg	
452	gtagccttccta	
453	cggtagccttccta	
454	cacggtagccttccta	
455	agcacggtagccttccta	
456	gaacgctggaccttccat	
457	gaccttccat	
458	tggaccttccat	
459	gctggaccttccat	
460	acgctggaccttccat	
461	taagctctgtcaacgccagg	
462	gagaacgctggaccttccatgt	
463	tccatgtcggctcctgatgct	
464	ttcatgccttgcaaaatggcg	
465	tgctagctgtgcctgtacct	
466	agcatcaggaccgacatgga	
467	gaccttccatgtcggctcctgat	
468	acaaccacgagaacgggaac	
469	gaaccttccatgctgttccg	
470	caatcaatctgaggagaccc	
471	tcagctctggtaacttttca	
472	tggttacggctctgtcccatg	



473	gtctatcggaggactggcgc	
474	cattttacgggaggcgggc	
475	gaggggaccattttacgggc	
476	tgtccagccgaggggaccat	
477	cgggcttacggcgatgctg	
478	tggaccttctatgtcgggtcc	
479	tgtcccatgtttttagaagc	
480	gtggttacggtcgtgcccat	
481	cctccaaatgaaagaccccc	
482	ttgtactctccatgatgggt	
483	ttccatgctgttccggtgg	
484	gaccttctatgtcgggtcctg	
485	gagaccgctcgaccttcgat	
486	ttgccccatattttagaac	
487	ttgaaactgaggtgggac	
488	ctatcggaggactggcgcgcc	
489	cttgagggcctcccgggcg	
490	gctgaaccttccatgctgtt	
491	tagaaacagcattcttcttttagggcagcaca	
492	agatgggtctcagataaagcgaa	
493	ttccgctttatctgagaacctct	
494	gtcccaggttgatagaggctgc	
495	gcgccagtccctccgatagac	
496	atcggaggactggcgcgccg	
497	ggtctgtcccatatttttag	
498	tttttcaacggtgagggggg	sos
499	tttttcaagcgttgatttttt	sos
500	gggggtcaacggttgatttttt	sos
501	gggggttttcaacggtttgagggggg	sos
502	ggttacggtctgtcccatat	
503	ctgtcccatatttttagaca	
504	accatcctgaggccattcgg	
505	cgtctatcgggcttctgtgtctg	
506	ggccatcccacattgaaagt	
507	ccaaatatcggtggtcaagcac	
508	gtgcttgaccaccgatatttgg	
509	gtgctgatcaccgatctctgttcgg	
510	ggccaaactttcaatgtggatggcctc	
511	ttccgcccgaatggcctcaggatgggtac	
512	tatagtccctgagactgccccaccttctcaacaacc	
513	gcagcctctatacaacctgggacggga	
514	ctatcggaggactggcgcgccg	
515	tatcggaggactggcgcgccg	
516	gatcggaggactggcgcgccg	
517	ccgaacaggatatcggtgatcagcac	
518	ttttggggtcaacggttgagggggg	
519	gggggtcaacggttgagggggg	sos
520	cgcgcgcgcgcgcgcgcgcg	s
521	ggggcatgacgttcggggggg	ss
522	ggggcatgacgttcaaaaaa	s
523	ggggcatgagcttcggggggg	s
524	ggggcatgacgttcggggggg	sos
525	aaaacatgacgttcaaaaaa	sos
526	aaaacatgacgttcggggggg	sos
527	ggggcatgacgttcaaaaaa	sos
528	accatggacgatctgtttccctc	s
529	gccatggacgaactgttccccctc	s

530	cccccccccccccccc	SOS
531	gggggggggggggggg	SOS
532	gctgtaaaatgaatcgccg	SOS
533	ttcgggcggactcctccatt	SOS
534	tatgccgcgcccggacttat	SOS
535	ggggtaatcgatcagggggg	SOS
536	tttgagaacgctggaccttc	SOS
537	gatcgctgatctaatactcg	SOS
538	gtcggtcctgatgctgttcc	SOS
539	tcgtcgtcagttcgtctcg	SOS
540	ctggaccttccatgtcgg	SOS
541	gctcgttcagcgcgtct	SOS
542	ctggaccttccatgtc	SOS
543	caactgtccttcgtcga	SOS
544	cgctggaccttccatgtcgg	SOS
545	gctgagctcatgcgtctgc	SOS
546	aacgctggaccttccatgtc	SOS
547	tgcataccgtacacagctct	SOS
548	ccttccatgtcggtcctgat	SOS
549	tactcttcggatcccttgcg	SOS
550	ttccatgtcggtcctgat	SOS
551	ctgattgctctctcgtga	SOS
552	ggcgttattcctgaactgcc	O
553	cctacgttgtatgcgccagct	O
554	ggggtaatcgatgagggggg	O
555	ttcgggcggactcctccatt	O
556	tttttttttttttttttt	O
557	gggggtttttttttggggg	O
558	tttttgggggggggttttt	O
559	gggggggggggggggggt	O
560	aaaaaaaaaaaaaaaaaaaa	O
561	cccccaaaaaaaaaaccccc	O
562	aaaaaccccccccccaaaaa	O
563	tttgaattcaggactgggtgaggtgag	O
564	tttgaatcctcagcggctcctcagtggc	O
565	aattctctatcggggcttctgtgtctgttggttccgctttat	O
566	ctagataaaagcggaaccagcaacagacacagaagccccgatagag	O
567	ttttctagagaggtgcacaaatgctctgg	O
568	tttgaattccgtgtacagaagcgagaagc	O
569	tttgccgcttagacttaacctgagagata	O
570	tttggccacagagagacagagacacttc	O
571	tttggcccgcttctcgttctgtacacg	O
572	gagaacgctggaccttccat	S
573	tccatgtcggtcctgatgct	S
574	ctgtcg	S
575	tcgtga	S
576	cgtcga	S
577	agtgc	S
578	ctgtcg	O
579	agtgc	O
580	cgtcga	O
581	tcgtga	O
582	gagaacgctccagcttcgat	O
583	gctagacgtaagcgtga	O
584	gagaacgctcgaccttccat	O
585	gagaacgctggacctatccat	O
586	gctagaggttagcgtga	O

587	gagaacgctggacttccat	o
588	tcacgctaacgtctagc	o
589	bgctagacggttagcgtga	o
590	atggaaggctcgacggttctc	o
591	gagaacgctggaccttcgat	o
592	gagaacgatggaccttccat	o
593	gagaacgctggatccat	o
594	gagaacgctccagcactgat	o
595	tccatgtcggctcctgctgat	o
596	atgtcctcggctcctgatgct	o
597	gagaacgctccaccttccat	o
598	gagaacgctggaccttcgta	o
599	batggaaggctccagcgttctc	o
600	tcctga	o
601	tcaacggt	o
602	aacggt	o
603	aacggtga	o
604	tcacgctaacctctagc	o
605	gagaacgctggaccttgcat	o
606	gctggaccttccat	o
607	gagaacgctggacctcatccat	o
608	gagaacgctggacgctcatccat	o
609	aacggtgaggggcat	o
610	atgccctcaacggt	o
611	tcaacggtga	o
612	gctggaccttccat	o
613	caacggt	o
614	acaacggtga	o
615	tcacgt	o
616	tcaagctt	o
617	tcgtca	o
618	aggatatc	o
619	tagacgtc	o
620	gacgtcat	o
621	ccatcgat	o
622	atcgatgt	o
623	atgcatgt	o
624	ccatgcat	o
625	agcgctga	o
626	tcagcgct	o
627	ccttcgat	o
628	gtgccggggtctccgggc	s
629	gctgtggggcggtcctg	s
630	btcaacggt	o
631	ftcaacggt	o
632	faacggtga	o
633	tcaacgt	s
634	aacggtg	s
635	cgacga	o
636	tcaacggt	o
637	tcgga	o
638	agaacggt	o
639	tcacgat	o
640	taaacggt	s
641	ccaacggt	s
642	gctcga	s
643	cgacgt	s

- 31 -

644	cgtcgt	s
645	acgtgt	s
646	cgttcg	s
647	gagcaagctggaccttccat	s
648	cgcgta	s
649	cgtacg	s
650	tcaccggt	s
651	caagagatgctaacaatgca	s
652	acccatcaatagctctgtgc	s
653	ccatcgat	o
654	tcgacgtc	o
655	ctagcgct	o
656	taagcgct	o
657	tcgcgaattcgcg	o
658	atggaaggtccagcgttct	o
659	actggacgttagcgtga	o
660	cgcctggggctggtctgg	o
661	gtgtcggggtctccgggc	o
662	gtgccggggtctccgggc	o
663	cgccgtcgcggcggttgg	o
664	gaagttcacgttgaggggcat	o
665	atctggtgagggcaagctatg	s
666	gttgaaaccgagaaacatcat	s
667	gcaacgtt	o
668	gtaacgtt	o
669	cgaacgtt	o
670	gaaacgtt	o
671	caaacgtt	o
672	ctaacgtt	o
673	ggaacgtt	o
674	tgaacgtt	o
675	acaacgtt	o
676	ttaacgtt	o
677	aaaacgtt	o
678	ataacgtt	o
679	aacgttct	o
680	tccgatcg	o
681	tccgtacg	o
682	gctagacgctagcgtga	o
683	gagaacgctggacctcatccat	o
684	gagaacgctagaccttctat	o
685	actagacgttagtgtga	o
686	cacaccttggtcaatgtcacgt	o
687	tctccatcctatggttttatcg	o
688	cgctggaccttccat	o
689	caccaccttggtcaatgtcacgt	o
690	gctagacgttagcgtga	o
691	agtgcgattgcagatcg	o
692	ttttcgttttgtggtttgtggtt	
693	ttttcgttttgtcgttttgtcggt	
694	ttttgtttttgtggtttgtggtt	
695	accgcatggattctaggcca	s
696	gctagacgttagcgt	o
697	aacgctggaccttccat	o
698	tcaazggt	o
699	ccttcgat	o
700	actagacgttagtgtga	s

- 32 -

701	gctagaggtttagcgtga	s
702	atggactctccagcggttctc	o
703	atcgactctcgagcggttctc	o
704	gctagacggttagc	o
705	gctagacgt	o
706	agtgcgattcgagatcg	o
707	tcagzgct	o
708	ctgattgctctctcgtga	o
709	tzaacggt	o
710	gagaazgctggaccttccat	o
711	gctagacggttaggctga	o
712	gctacttagcgtga	o
713	gctaccttagcgtga	o
714	atcgacttcgagcggttctc	o
715	atgcactctgcagcggttctc	o
716	agtgactctccagcggttctc	o
717	gccagatggttagctgga	o
718	atcgactcgagcggttctc	o
719	atcgatcgagcggttctc	o
720	bgagaacgctcgaccttcgat	o
721	gctagacggttagctgga	sos
722	atcgactctcgagcggttctc	sos
723	tagacggttagcgtga	o
724	cgactctcgagcggttctc	o
725	ggggtcgaccttggagggggg	sos
726	gctaacggttagcgtga	o
727	cgtcgctcgt	o
728	gagaacgctggacztccat	o
729	atcgacctacgtgcgttztc	o
730	atzgacctacgtgcgttctc	o
731	gctagazggttagcgt	o
732	atcgactctcgagzggttctc	o
733	ggggtaatgcatcagggggg	sos
734	ggctgtattcctgactgcc	s
735	ccatgctaacctctagc	o
736	gctagatggttagcgtga	o
737	cgtaccttacggtga	o
738	tccatgctggtcctgatgct	o
739	atcgactctctcgagcggttctc	o
740	gctagagcttagcgtga	o
741	atcgactctcgagtgttctc	o
742	aacgctcgaccttcgat	o
743	ctcaacgctggaccttccat	o
744	atcgacctacgtgcgttctc	o
745	gagaatgctggaccttccat	o
746	tcacgctaacctctgac	o
747	bgagaacgctccagcactgat	o
748	bgagcaagctggaccttccat	o
749	cgctagagggttagcgtga	o
750	gctagatggttaacgt	o
751	atggaaggtccacggttctc	o
752	gctagatggttagcgt	o
753	gctagacggttagtgt	o
754	tccatgacggtcctgatgct	o
755	tccatggcggtcctgatgct	o
756	gctagacgatagcgt	o
757	gctagtcgatagcgt	o

- 33 -

758	tccatgacgttcctgatgct	o
759	tccatgtcggttcctgatgct	o
760	gctagacgttagzgt	o
761	gctaggcggttagcgt	o
762	tccatgtzgggtcctgatgct	o
763	tccatgtcggtzctgatgct	o
764	atzgactctzgagzgttctc	o
765	atggaaggtccagtgttctc	o
766	gcatgacgttgagct	o
767	gggggtcaacgttgagggggg	s
768	gggggtcaagtctgagggggg	sos
769	cgcgcgcgcgcgcgcgcgcg	o
770	cccccccccccccccccccccccc	s
771	cccccccccccccccccccccccc	s
772	tccatgtcgctcctgatcct	o
773	gctaaacgttagcgt	o
774	tccatgtcgatcctgatgct	o
775	tccatgccggtcctgatgct	o
776	aaaatcaacgttgaaaaaa	sos
777	tccataacgttcctgatgct	o
778	tggaggtcccaccgagatcgag	o
779	cgtcgtcgtcgtcgtcgtcg	s
780	ctgctgctgctgctgctgctg	s
781	gagaacgctccgaccttcgat	s
782	gctagatgttagcgt	s
783	gcatgacgttgagct	s
784	tcaatgctgaf	o
785	tcaacgttgaf	o
786	tcaacgttgab	o
787	gcaatattgcb	o
788	gcaatattgcf	o
789	agttgcaact	o
790	tcttcgaa	o
791	tcaacgtc	o
792	ccatgtcggtcctgatgct	o
793	gtttttatataatttggg	o
794	tttttgtttgctggtttgctg	o
795	ttgggggggggtt	s
796	gggggttgggggtt	s
797	ggtggtgtaggttttgg	o
798	bgagaazgctcgaccttcgat	o
799	tcaacgttaacgttaacgtt	o
800	bgagcaagztggaccttccat	o
801	bgagaazgctccagcactgat	o
802	tcaazgttgax	o
803	gzaatattgcx	o
804	tgctgcttttgcgttttgcgtt	o
805	ctgcgttagcaatttaactgtg	o
806	tccatgacgttcctgatgct	s
807	tgcattgccgtgcattccgtacacagctct	s
808	tgcattgccgtacacagctct	s
809	tgcattcagctct	s
810	tgcgtctct	s
811	cccccccccccccccccccc	s
812	cccccccccccc	s
813	cccccccc	s
814	tgcattcagctct	sos

- 34 -

815	tgcacgcccgtacacagctct	o
816	gagcaagctggaccttccat	s
817	tcaacgttaacgttaacgttaacgttaacgtt	s
818	gagaacgctcgaccttcgat	s
819	gtccccatttcccagaggaggaaat	o
820	ctagcggctgacgtcatcaagctag	o
821	ctagcttgatgacgtcagccgctag	o
822	cggctgacgtcatcaa	s
823	ctgacgtg	o
824	ctgacgtcat	o
825	attcgatcggggcggggcgag	o
826	ctcggcccgcccgatcgaat	o
827	gactgacgtcagcgt	o
828	ctagcggctgacgtcataaagctagc	s
829	ctagctttatgacgtcagccgctagc	s
830	ctagcggctgagctcataaagctagc	s
831	ctagtggctgacgtcatcaagctag	s
832	tccaccacgtggtctatgct	s
833	gggaatgaaagattttattataag	o
834	tctaaaaaccatctattcttaaccct	o
835	agctcaacgtcatgc	o
836	ttaacgggtggttagcgggtattggtc	o
837	ttaagaccaataaccgctaccaccg	o
838	gatctagtgatgagtcagccggatc	o
839	gatccggctgactcatcactagatc	o
840	tccaagacgttctctgatgct	o
841	tccatgacgtccctgatgct	o
842	tccaccacgtggctgatgct	o
843	ccacgtggacctctagc	o
844	tcagaccaogtggtcggtgttctga	o
845	tcaggaacacccgaccacgtggtctga	o
846	catttccacgatttccca	o
847	ttctctctgcaagagact	o
848	tgtatctctctgaaggact	o
849	ataaagcgaactagcagcagtttc	o
850	gaaactgctgctagtttcgctttat	o
851	tgcccaaagaggaaaaatttgtttcatacag	o
852	ctgtatgaaacaaatttctcttttgggca	o
853	ttagggttaggggttaggggt	s
854	tccatgagcttctctgatgct	s
855	aaaacatgacgttcaaaaaa	s
856	aaaacatgacgttcgggggg	s
857	ggggcatgagcttcgggggg	sos
858	ctagcgtgacgtcatcaagctagt	o
859	tctgacgtcatctgacgttggtgacgtct	o
860	ggaattagtaataagatatagaagtt	o
861	tttaccttttataaacataactaaaaaaa	o
862	gcgtttttttttgcg	s
863	atatctaatacaaaacattaacaaa	o
864	tctatcccagggtggttctctgttag	o
865	btccatgacgttctctgatgct	o
866	btccatgagcttctctgatgct	o
867	tttttttttttttf	o
868	tttttttttttttf	so
869	ctagcttgatgagctcagccgctag	o
870	ttcagttgtcttgctgcttagctaa	o
871	tccatgagcttctctgatgct	s

- 35 -

872	ctagcggctgacgtcatcaatctag	o
873	tgctagctgtgcctgtacct	s
874	atgctaaaggacgtcacattgca	o
875	tgcaatgtgacgtccttttagcat	o
876	gtaggggactttccgagctcgagatcctatg	o
877	cataggatctcgagctcggaaagtcccctac	o
878	ctgtcaggaactgcaggtaagg	o
879	cataacataggaatatttactcctcgc	o
880	ctccagctccaagaaaggacg	o
881	gaagtttctggtaagtcttcg	o
882	tgctgcttttgtgcttttgtgctt	s
883	tcgtcgttttgtggttttgtggtt	s
884	tcgtcgtttgtcgttttgtcgtt	s
885	tcctgacgttcggcgcgcgccc	s
886	tgctgcttttgtgcttttgtgctt	
887	tccatgagcttcctgagctt	s
888	tcgtcgtttcgtcgttttgacgtt	s
889	tcgtcgtttgcgtgcgtttcgtcgtt	s
890	tcgcgtgcgttttgcgttttgacgtt	s
891	ttcgtcgttttgcgttttgcgtt	s
892	tcctgacggggaagt	s
893	tcctggcgtggaagt	s
894	tcctggcgtggaagt	s
895	tcctggcgtggaagt	s
896	tcctgacgtggaagt	s
897	gcgacgttcggcgcgcgccc	s
898	gcgacggcgcgcgcgcgccc	s
899	gcggcgtcggcgcgcgcgccc	s
900	gcggcgtcggcgcgcgcgccc	s
901	gcgacggtcggcgcgcgccc	s
902	gcggcgttcggcgcgcgccc	s
903	gcgacgtcggcgcgcgccc	s
904	tcgtcgtctgtctcgc	s
905	tgtgggggttttgggttttgg	s
906	aggggaggggaggggagggg	s
907	tgtgtgtgtgtgtgtgtgtgt	s
908	ctctctctctctctctctct	sos
909	ggggtcgacgtcgagggggg	s
910	atatatatatatatatatat	s
911	tttttttttttttttttttttt	s
912	tttttttttttttttttttt	s
913	tttttttttttttttttt	s
914	gctagaggggaggggt	
915	gctagatgttagggg	
916	gcatgagggggagct	
917	atggaaggtccagggggctc	
918	atggactctggagggggctc	
919	atggaaggtccaaggggctc	
920	gagaaggggggaccttgat	
921	gagaaggggggaccttccat	
922	gagaagggggccagcactgat	
923	tccatgtggggcctgatgct	
924	tccatgaggggcctgatgct	
925	tccatgtggggcctgatgat	
926	atggactctccgggggtctc	
927	atggaaggtccgggggtctc	
928	atggactctggaggggtctc	



- 36 -

929	atggaggctccatggggctc	
930	atggactctggggggttctc	
931	tccatgtgggtggggatgct	
932	tccatgcggtggggatgct	
933	tccatgggggtcctgatgct	
934	tccatgggggtccctgatgct	
935	tccatgggggtgcctgatgct	
936	tccatgggggttcctgatgct	
937	tccatcgggggcctgatgct	
938	gctagaggagtggt	
939	tttttttttttttttttt	s
940	gmgtcaacgttgaggmggg	s
941	ggggagttcggtgagggggg	s
942	tcgtcgtttccccccccc	s
943	ttggggggttttttttttt	s
944	tttaaattttaaaatttaata	s
945	ttggtttttttggtttttttg	s
946	tttccottttcccttttccctc	s
947	ggggtcatcgatgagggggg s	sos
948	tccatgacgttcctgacgtt	
949	tccatgacgttcctgacgtt	
950	tccatgacgttcctgacgtt	
951	tccatgacgttcctgacgtt	
952	tccatgacgttcctgacgtt	
953	tccatgacgttcctgacgtt	
954	tccatgacgttcctgacgtt	
955	tccatgacgttcctgacgtt	
956	tccatgacgttcctgacgtt	
957	tccatgacgttcctgacgtt	
958	tccatgacgttcctgacgtt	
959	gggggacgatcgtcggggg	sos
960	gggggtcgtagacggggg	sos
961	tttttttttttttttttt	po
962	aaaaaaaaaaaaaaaaaaaaa	po
963	cccccccccccccccccccc	po
964	tcgtcgttttgtcgttttgtcg	
965	tcgtcgttttgtcgttttgtcg	
966	tcgtcgttttgtcgttttgtcg	
967	tcgtcgttttgtcgttttgtcg	
968	ggggtcaacgttgagggggg	
969	ggggtcaacgttgagggggg	
970	ggggtcaagcttgagggggg	
971	tgctgottccccccccccc	
972	ggggacgtcgacgtgggggg	sos
973	ggggtcgtcgacgagggggg	sos
974	ggggtcgacgtacgtcgagggg	sos
975	ggggaccggtaccggtggggg	sos
976	gggtcgacgtcgagggggg	sos
977	ggggtcgacgtcgagggggg	sos
978	ggggaacgttaacgttggggg	sos
979	ggggtcaccggtgagggggg	sos
980	ggggtcggttcgaacgagggg	sos

- 37 -

981	ggggacgttcgaacgtgggggg	sos
982	tcaactttga	s
983	tcaagcttga	s
984	tcacgatcgtga	s
985	tcagcatgctga	s
986	gggggagcatgctggggggg	sos
987	gggggggggggggggggggg	sos
988	gggggacgatatcgctcgggggg	sos
989	gggggacgacgtcgctcgggggg	sos
990	gggggacgagctcgctcgggggg	sos
991	gggggacgtacgtcgggggg	sos
992	tcaacgtt	
993	tccataccggtcctgatgct	
994	tccataccggtcctaccggt	s
995	gggggacgatcggtgggggg	sos
996	ggggaacgatcgctcgggggg	sos
997	ggg ggg acg atc gtc ggg ggg	sos
998	ggg gga cga tcg tcg ggg ggg	sos
999	aaa gac gtt aaa	po
1000	aaagagcttaaa	po
1001	aaagazgttaaa	po
1002	aaattcggaana	po
1003	gggggtcatcgatgagggggg	sos
1004	gggggtcaacgttgagggggg	sos
1005	atgtagcttaataacaaagc	po
1006	ggatcccttgagttacttct	po
1007	ccattccacttctgattacc	po
1008	tatgtattatcatgtagata	po
1009	agcctaogtattcaccctcc	po
1010	ttcctgcaactactattgta	po
1011	atagaaggccctacaccagt	po
1012	ttacaccggtctatggaggt	po
1013	ctaaccagatcaagtctagg	po
1014	cctagacttgatctggtag	po
1015	tataagcctcgctccgacatg	po
1016	catgtcggacgaggcttata	po
1017	tgggtggtggggagtaagctc	po
1018	gagctactccccaccacca	po
1019	gccttogatcttcggttgga	po
1020	tggacttctctttgccgtct	po
1021	atgctgtagcccagcgataa	po
1022	accgaatcagcggaaagtga	po
1023	tccatgacgttcctgacgtt	
1024	ggagaaacccatgagctcatctgg	
1025	accacagaccagcaggcaga	
1026	gagcgtgaactgcgcgaaga	
1027	tcggtacccttgacgcggtt	
1028	ctggagccctagccaaggat	
1029	gcgactccatcaccagcgat	
1030	cctgaagtaagaaccagatgt	

- 38 -

1031	ctgtgttatctgacatacacc	
1032	aattagccttaggtgattggg	
1033	acatctgggtcttacttcagg	
1034	ataagtcataattttgggaactac	
1035	cccaatcacctaaggctaatt	
1036	ggggtcgtcgacgagggggg	sos
1037	ggggtcgttcgaacgagggggg	sos
1038	ggggacgttcgaacgtgggggg	sos
1039	tcctggcgqggaagt	s
1040	ggggaacgacgtcggtgggggg	sos
1041	ggggaacgtacgtcgggggg	sos
1042	ggggaacgtacgtacgtgggggg	sos
1043	ggggtcaccggtgagggggg	sos
1044	ggggtcgacgtacgtcgaggggg	sos
1045	ggggaccggtaccggtgggggg	sos
1046	gggtcgacgtcgagggggg	sos
1047	ggggtcgacgtcgagggg	sos
1048	ggggaacgttaacgtgggggg	sos
1049	ggggacgtcgacgtggggg	sos
1050	gcactcttcgaagctacagccggcagcctctgat	
1051	cggctcttccatgaggtctttgctaattcttg	
1052	cggctcttccatgaaagtcttggacgatgtgagc	
1053	tcctgcagggttaagt	s
1054	gggggtcggtcggtgggggg	sos
1055	gggggatgattggtgggggg	sos
1056	gggggatzgatzggtgggggg	sos
1057	gggggagctagcttgggggg	sos
1058	ggttcttttggtccttgtct	s
1059	ggttcttttggtcctcgtct	s
1060	ggttcttttggtccttatct	s
1061	ggttcttggttctccttgtct	s
1062	tggcttttggtccttgtct	s
1063	ggttcaaatggtccttgtct	s
1064	gggtcttttgggccttgtct	s
1065	tccaggacttctctcaggtttttt	s
1066	tccaaaacttctctcaaatt	s
1067	tactacttttatacttttatactt	s
1068	tgtgtgtgtgtgtgtgtgtgtg	s
1069	ttgttggtgtgtgtgtgtgtgtg	s
1070	ggctccggggaggggaatttttgtctat	s
1071	gggacgatcgtcggggggg	sos
1072	gggtcgtcgacgaggggggg	sos
1073	ggtcgtcgacgaggggggg	sos
1074	gggtcgtcgtcggtgggggg	sos
1075	ggggacgatcgtcggggggg	sos
1076	ggggacgtcgtcggtgggggg	sos
1077	ggggtcgacgtcgacgtcgaggggggg	sos
1078	ggggaaccgcggttggggggg	sos
1079	ggggacgacgtcggtggggggg	sos
1080	tcgtcgtcgtcgtcggtggggggg	sos

- 39 -

1081	tcctgccggggaagt	s
1082	tcctgcaggggaagt	s
1083	tcctgaaggggaagt	s
1084	tcctggcgggcaagt	s
1085	tcctggcgggtaagt	s
1086	tcctggcgggaaagt	s
1087	tccggcggggaagt	s
1088	tcggggcggggaagt	s
1089	tcccggcggggaagt	s
1090	gggggacgttggggg	s
1091	gggggtttttttttggggg	sos
1092	ggggccccccccggggg	sos
1093	ggggttgttgttgttggggg	sos

Nucleic acids having modified backbones also are included in the class of nucleic acids having antiangiogenic properties. Modified backbone nucleic acids include those having phosphorothioate, methylphosphonate, methylphosphorothioate, p-ethoxy and/or phosphorodithioate internucleotide or internucleoside bonds. Chimeric oligonucleotides having mixtures of modified and/or unmodified backbones also are included in the invention.

In the case when an antiangiogenic nucleic acid is administered in conjunction with a nucleic acid vector, it is preferred that the backbone of the antiangiogenic nucleic acid be a chimeric combination of phosphodiester and phosphorothioate bonds (or other modification of the internucleotide bonds). This is because the uptake of the plasmid vector by the cell may be hindered by the presence of completely phosphorothioate oligonucleotide. Thus when both a vector and an oligonucleotide are delivered to a subject, it is preferred that the oligonucleotide have chimeric or phosphorothioate internucleotide bonds and that the plasmid be associated with a vehicle that delivers it directly into the cell, thus avoiding the need for cellular uptake. Such vehicles are known in the art and include, for example, liposomes, electroporation devices and gene guns.

For use in the instant invention, the antiangiogenic nucleic acids can be synthesized *de novo* using any of a number of procedures well known in the art. Such compounds are referred to as "synthetic nucleic acids." For example, the b-cyanoethyl phosphoramidite method (Beaucage, S.L., and Caruthers, M.H., *Tet. Let.* 22:1859, 1981); nucleoside H-phosphonate method (Garegg *et al.*, *Tet. Let.* 27:4051-4054, 1986; Froehler *et al.*, *Nucl. Acid. Res.* 14:5399-5407, 1986, Garegg *et al.*, *Tet. Let.* 27:4055-4058, 1986, Gaffney *et al.*, *Tet. Let.* 29:2619-2622, 1988). These chemistries can be performed by a variety of automated oligonucleotide synthesizers available in the market.

- 40 -

Alternatively, nucleic acids can be produced on a large scale in plasmids, (see, e.g., Sambrook, *et al.*, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press, New York, 1989) and separated into smaller pieces or administered whole. Nucleic acids can be prepared from existing nucleic acid sequences (e.g., genomic or cDNA) using known techniques, such as those employing restriction enzymes, exonucleases or endonucleases. Nucleic acids prepared in this manner are referred to as isolated nucleic acids. The term "antiangiogenic nucleic acid" encompasses both synthetic and isolated antiangiogenic nucleic acids.

For use *in vivo*, nucleic acids are preferably relatively resistant to degradation (e.g., are stabilized). A "stabilized nucleic acid molecule" as used herein means a nucleic acid molecule that is relatively resistant to *in vivo* degradation (e.g. via an exo- or endo-nuclease). Stabilization can be a function of length or secondary structure. Antiangiogenic nucleic acids that are tens to hundreds of kilobases long are relatively resistant to *in vivo* degradation. For shorter antiangiogenic nucleic acids, secondary structure can stabilize and increase their effect. For example, if the 3' end of a nucleic acid is self-complementary to an upstream region of the same nucleic acid, so that it can fold back and form a stem/loop structure by internal self-hybridization, then the nucleic acid may be stabilized and therefore may exhibit more *in vivo* activity.

Alternatively, nucleic acid stabilization can be accomplished via backbone modifications. Preferred stabilized nucleic acids of the instant invention have a modified backbone. It has been demonstrated that modification of the nucleic acid backbone provides enhanced activity of the antiangiogenic nucleic acids when administered *in vivo*. One type of modified backbone is a phosphate backbone modification. For example, antiangiogenic nucleic acids including at least two phosphorothioate linkages at the 5' end of the oligonucleotide and multiple phosphorothioate linkages at the 3' end, preferably 5 or more, can in some circumstances protect the nucleic acid from degradation by intracellular exo- and endo-nucleases and thereby provide maximal activity. Other phosphate modified nucleic acids include phosphodiester modified nucleic acids, combinations of phosphodiester and phosphorothioate nucleic acids, methylphosphonate, methylphosphorothioate, phosphorodithioate, p-ethoxy and combinations thereof. Some of these combinations in CpG nucleic acids and their particular effects on immune cells is discussed in more detail in PCT Published Patent Applications PCT/US95/01570 and PCT/US97/19791, the entire contents of which are hereby incorporated by reference. Although not intending to be bound by any

- 41 -

particular theory, it is believed that these modified nucleic acids may have increased activity relative to unmodified nucleic acids due to enhanced nuclease resistance, increased cellular uptake, increased protein binding, and/or altered intracellular localization.

Modified backbone nucleic acids, such as those having phosphorothioates bonds may be synthesized using automated techniques employing, for example, phosphoramidate or H-phosphonate chemistries. Aryl- and alkyl-phosphonates can be made, e.g., as described in U.S. Patent No. 4,469,863. Alkylphosphotriesters, in which the charged oxygen moiety is alkylated as described in U.S. Patent No. 5,023,243 and European Patent No. 092,574, can be prepared by automated solid phase synthesis using commercially available reagents. Methods for making other nucleic acid backbone modifications and substitutions have been described (Uhlmann, E. and Peyman, A., *Chem. Rev.* 90:544, 1990; Goodchild, J., *Bioconjugate Chem.* 1:165, 1990).

Another type of modified backbone, useful according to the invention, is a peptide nucleic acid. The backbone is composed of aminoethylglycine and supports bases which provide the nucleic acid character. The backbone does not include any phosphate and thus may optionally have no net charge. The lack of charge allows for stronger DNA-DNA binding because the charge repulsion between the two strands does not exist. Additionally, because the backbone has an extra methylene group, the oligonucleotides are enzyme/protease resistant. Peptide nucleic acids can be purchased from various commercial sources, e.g., Perkin Elmer, or synthesized de novo.

Another class of backbone modifications include 2'-O-methylribonucleosides (2'-O-Me). These types of substitutions are described extensively in the literature and in particular with respect to their immunostimulating properties in Zhao et al., *Bioorganic and Medicinal Chemistry Letters*, 1999, 9:24:3453. Zhao et al. describes methods of preparing 2'-O-Me modifications to nucleic acids.

The nucleic acid molecules of the invention may include naturally-occurring or synthetic purine or pyrimidine heterocyclic bases as well as modified backbones. Purine or pyrimidine heterocyclic bases include, but are not limited to, adenine, guanine, cytosine, thymidine, uracil, and inosine. Other representative heterocyclic bases are disclosed in US Patent No. 3,687,808, issued to Merigan, et al. The terms "purines" or "pyrimidines" or "bases" are used herein to refer to both naturally-occurring or synthetic purines, pyrimidines or bases.

- 42 -

Other stabilized nucleic acids include non-ionic DNA analogs, such as alkyl- and aryl-phosphates (in which the charged phosphonate oxygen is replaced by an alkyl or aryl group), phosphodiester and alkylphosphotriesters, in which the charged oxygen moiety is alkylated. Nucleic acids which contain diol, such as tetraethyleneglycol or hexaethyleneglycol, at either  
5 or both termini have also been shown to be substantially resistant to nuclease degradation.

The antiangiogenic nucleic acids having backbone modifications useful according to the invention in some embodiments are S- or R-chiral antiangiogenic nucleic acids. An "S chiral antiangiogenic nucleic acid" as used herein is an antiangiogenic nucleic acid wherein at least two nucleotides have a backbone modification forming a chiral center and wherein a  
10 plurality of the chiral centers have S chirality. An "R chiral antiangiogenic nucleic acid" as used herein is an antiangiogenic nucleic acid wherein at least two nucleotides have a backbone modification forming a chiral center and wherein a plurality of the chiral centers have R chirality. The backbone modification may be any type of modification that forms a chiral center. The modifications include but are not limited to phosphorothioate,  
15 methylphosphonate, methylphosphorothioate, phosphorodithioate, p-ethoxy, 2'-O-Me and combinations thereof.

The chiral antiangiogenic nucleic acids must have at least two nucleotides within the nucleic acid that have a backbone modification. All or less than all of the nucleotides in the nucleic acid, however, may have a modified backbone. Of the nucleotides having a modified  
20 backbone (referred to as chiral centers), a plurality have a single chirality, S or R. A "plurality" as used herein refers to an amount greater than 50%. Thus, less than all of the chiral centers may have S or R chirality as long as a plurality of the chiral centers have S or R chirality. In some embodiments at least 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100% of the chiral centers have S or R chirality. In other embodiments at least 55%, 60%,  
25 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100% of the nucleotides have backbone modifications.

The S- and R- chiral antiangiogenic nucleic acids may be prepared by any method known in the art for producing chirally pure oligonucleotides. Stec et al teach methods for producing stereopure phosphorothioate oligodeoxynucleotides using an oxathiaphospholane.  
30 (Stec, W.J., et al., 1995, *J. Am. Chem. Soc.*, 117:12019). Other methods for making chirally pure oligonucleotides have been described by companies such as ISIS Pharmaceuticals. US Patents which disclose methods for generating stereopure oligonucleotides include 5,883,237;

- 43 -

5,837,856; 5,599,797; 5,512,668; 5,856,465; 5,359,052; 5,506,212; 5,521,302; and 5,212,295, each of which is hereby incorporated by reference in its entirety.

As used herein, administration of an antiangiogenic nucleic acid is intended to embrace the administration of one or more antiangiogenic nucleic acids which may or may not differ in terms of their profile, sequence, backbone modifications and biological effect. As an example, CpG nucleic acids and T-rich nucleic acids may be administered to a single subject along with other antiangiogenic medicament(s), such as endostatin or angiostatin. In another example, a plurality of CpG nucleic acids which differ in nucleotide sequence may also be administered to a subject.

The invention encompasses the administration of the antiangiogenic nucleic acids along with other medicaments in order to provide a synergistic effect useful in the prevention and/or treatment of conditions that involve unwanted angiogenesis, such as cancer. Accordingly, methods for inhibition of angiogenesis are provided. The methods include the administration of at least one antiangiogenic nucleic acid formulated for administration to a subject. Non-nucleic acid antiangiogenesis molecules also can be administered to the subject, including, but not limited to endogenous angiogenesis inhibitors including PD 174073 and PD 166285 (Parke-Davis), SU5416 and SU6668 (Sugen), ZD 4190 and ZD 6474 (Zeneca), PTK 787 (also known as CGP79787 or ZK22584) (Novartis), Anti-VEGF mAb (Genentech), Anti-KDR mAb (ImClone), RPI 4610 (Ribozyme), TNP 470 (Abbott/TAP), AG 3340 (Agouron), Marimastat (British Biotech), Bay 12-9566 (Bayer), Neovastat (Aeterna), BMS 275291 (Bristol Myers-Squibb), CGS 27023A (Novartis), D1927 Chiroscience, D2163 (Chiroscience), Isoquinolines (Pfizer), Vitaxin (IXSYS), S-137 (Searle), S-836 (Searle), SM256 (Dupont), SG545 (Dupont), Angiostatin (EntreMed), Endostatin (EntreMed), Thalidomide (EntreMed), Squalamine (Magainin), CAI (National Cancer Institute), CM-101 (CarboMed), U-995 (Gwo-Chyang GMP), Combretastatin A-4 (Oxigene), platelet factor-4, vasostatin, thrombospondin, tissue inhibitors of metalloproteinases (TIMPs), STI412 (Sun and McMahon, *Drug Discov. Today* 5(8):344-353, 2000; Klohs and Hamby, *Curr. Opin. Biotechnol.* 10:544-549, 1999), fumagillin, non-glucocorticoid steroids and heparin and heparin fragments and antibodies to one or more angiogenic peptides such as  $\alpha$ -FGF,  $\beta$ -FGF, VEGF, IL-8, and GM-CSF. Some of the foregoing may be administered in the form of nucleic acids encoding proteins; in each case the active agent is a protein and not the nucleic acid encoding the protein.



- 44 -

The antiangiogenic nucleic acid molecules of the invention can be administered concurrently with, or sequentially with, the non-nucleic acid antiangiogenesis molecules described above. Coadministration may be in the form of administration of a composition containing both kinds of antiangiogenic agents, or a plurality of compositions, each of which may contain one or more than one of the antiangiogenic agents.

The invention may be used in the treatment of cancer, but is not so limited. In these methods, an effective amount of at least one antiangiogenic nucleic acid is administered to a subject having cancer, or in other instances a subject at risk of developing cancer. Other non-nucleic acid antiangiogenesis molecules also can be administered, as described above. In addition, in certain embodiments of the invention, anticancer molecules are administered in combination with the antiangiogenesis molecules.

The compounds useful in the invention may be delivered in a mixture with anti-proliferative agents (particularly anticancer agents) which are not antiangiogenic nucleic acids. One of ordinary skill in the art is familiar with a variety of anti-proliferative agents which are used in the medical arts to treat proliferative diseases such as cancer. These anticancer agents may act by directly killing cells, such as cancer cells (i.e., direct action anticancer agents), or alternatively they may act by sensitizing cells to direct action anti-cancer agents (i.e., indirect action anti-cancer agents). Those of skill in the art will recognize the distinction and are familiar with agents of either class. Anticancer agents include, but are not limited to, the following sub-classes of compounds:

Antineoplastic agents such as: Acivicin; Aclarubicin; Acodazole Hydrochloride; Acronine; Adozelesin; Adriamycin; Aldesleukin ; Altretamine; Ambomycin; Ametantrone Acetate; Aminoglutethimide; Amsacrine; Anastrozole; Anthramycin; Asparaginase; Asperlin ; Azacitidine; Azetepa; Azotomycin; Batimastat; Benzodepa; Bicalutamide; Bisantrone Hydrochloride; Bisnafide Dimesylate; Bizelesin; Bleomycin Sulfate; Brequinar Sodium; Bropirimine ; Busulfan; Cactinomycin; Calusterone; Caracemide; Carbetimer; Carboplatin; Carmustine; Carubicin Hydrochloride; Carzelesin; Cedefingol; Chlorambucil; Cirolemycin ; Cisplatin; Cladribine; Crisnatol Mesylate; Cyclophosphamide ; Cytarabine ; Dacarbazine; DACA (N-[2-(Dimethyl-amino)ethyl]acridine-4-carboxamide); Dactinomycin; Daunorubicin Hydrochloride; Daunomycin; Decitabine; Dexormaplatin; Dezaguanine; Dezaguanine Mesylate; Diaziquone; Docetaxel; Doxorubicin; Doxorubicin Hydrochloride; Droloxifene; Droloxifene Citrate; Dromostanolone Propionate; Duazomycin; Edatrexate; Eflornithine Hydrochloride ; Elsamitrucin; Enloplatin; Enpromate; Epirpropidine; Epirubicin

Hydrochloride; Erbulozole; Esorubicin Hydrochloride; Estramustine; Estramustine Phosphate Sodium; Etanidazole; Ethiodized Oil I 131; Etoposide; Etoposide Phosphate; Etoprine; Fadrozole Hydrochloride; Fazarabine; Fenretinide; Floxuridine; Fludarabine Phosphate; Fluorouracil; 5-FdUMP; Flurocitabine; Fosquidone; Fostriecin Sodium; Gemcitabine; 5 Gemcitabine Hydrochloride; Gold Au 198 ; Hydroxyurea; Idarubicin Hydrochloride; Ifosfamide; Ilmofofosine; Interferon Alfa-2a ; Interferon Alfa-2b ; Interferon Alfa-n1; Interferon Alfa-n3; Interferon Beta- I a ; Interferon Gamma- I b; Iproplatin; Irinotecan Hydrochloride ; Lanreotide Acetate; Letrozole; Leuprolide Acetate ; Liarozole Hydrochloride; Lometrexol Sodium; Lomustine; Losoxantrone Hydrochloride; Masoprocol; Maytansine; 10 Mechllorethamine Hydrochloride; Megestrol Acetate; Melengestrol Acetate; Melphalan; Menogaril; Mercaptopurine; Methotrexate; Methotrexate Sodium; Metoprine; Meturedopa; Mitindomide; Mitocarcin; Mitocromin; Mitogillin; Mitomalcin; Mitomycin; Mitosper; Mitotane; Mitoxantrone Hydrochloride; Mycophenolic Acid; Nocodazole; Nogalamycin; Ormaplatin; Oxisuran; Paclitaxel; Pegaspargase; Peliomycin; Pentamustine; Peplomycin 15 Sulfate; Perfosfamide; Pipobroman; Pipsulfan; Piroxantrone Hydrochloride; Plicamycin; Plomestane; Porfimer Sodium; Porfiromycin ; Prednimustine; Procarbazine Hydrochloride; Puromycin; Puromycin Hydrochloride; Pyrazofurin; Riboprine; Rogletimide; Safingol ; Safingol Hydrochloride ; Semustine; Simtrazene; Sparfosate Sodium; Sparsomycin; Spirogermanium Hydrochloride; Spiromustine; Spiroplatin; Streptonigrin; Streptozocin; 20 Strontium Chloride Sr 89; Sulofenur; Talisomycin; Taxane; Taxoid; Tecogalan Sodium; Tegafur; Teloxantrone Hydrochloride; Temoporfin; Teniposide; Teroxirone; Testolactone; Thiamiprine; Thioguanine; Thiotepa; Thymitaq; Tiazofurin; Tirapazamine; Tomudex; TOP-53; Topotecan Hydrochloride; Toremifene Citrate; Trestolone Acetate; Triciribine Phosphate; Trimetrexate; Trimetrexate Glucuronate; Triptorelin; Tubulozole Hydrochloride; Uracil 25 Mustard; Uredepia; Vapreotide; Verteporfin; Vinblastine; Vinblastine Sulfate; Vincristine; Vincristine Sulfate; Vindesine; Vindesine Sulfate; Vinepidine Sulfate; Vinglycinat Sulfate; Vinleurosine Sulfate; Vinorelbine Tartrate; Vinrosidine Sulfate; Vinzolidine Sulfate; Vorozole; Zeniplatin; Zinostatin; Zorubicin Hydrochloride; 2-Chlorodeoxyadenosine; 2'-Deoxyformycin; 9-aminocamptothecin; raltitrexed; N-propargyl-5,8-dideazafolic acid; 2-chloro-2'-arabino-fluoro-2'-deoxyadenosine; 2-chloro-2'-deoxyadenosine; anisomycin; 30 trichostatin A; hPRL-G129R; CEP-751; linomide.

Other anti-neoplastic compounds include: 20-epi-1,25 dihydroxyvitamin D3; 5-ethynyluracil; abiraterone; aclarubicin; acylfulvene; adecypenol; adozelesin; aldesleukin;

- 46 -

ALL-TK antagonists; altretamine; ambamustine; amidox; amifostine; aminolevulinic acid; amrubicin; amsacrine; anagrelide; anastrozole; andrographolide; angiogenesis inhibitors; antagonist D; antagonist G; antarelix; anti-dorsalizing morphogenetic protein-1; antiandrogen, prostatic carcinoma; antiestrogen; antineoplaston; antisense oligonucleotides; aphidicolin  
5 glycinate; apoptosis gene modulators; apoptosis regulators; apurinic acid; ara-CDP-DL-PTBA; arginine deaminase; asulacrine; atamestane; atrimustine; axinastatin 1; axinastatin 2; axinastatin 3; azasetron; azatoxin; azatyrosine; baccatin III derivatives; balanol; batimastat; BCR/ABL antagonists; benzochlorins; benzoylstaurosporine; beta lactam derivatives; beta-alethine; betaclamycin B; betulinic acid; bFGF inhibitor; bicalutamide;  
10 bisantrene; bisaziridinylspermine; bisnafide; bistratene A; bizelesin; breflate; broprimine; budotitane; buthionine sulfoximine; calcipotriol; calphostin C; camptothecin derivatives (e.g., 10-hydroxy- camptothecin); canarypox IL-2; capecitabine; carboxamide-amino-triazole; carboxyamidotriazole; CaRest M3; CARN 700; cartilage derived inhibitor; carzelesin; casein kinase inhibitors (ICOS); castanospermine; cecropin B; cetorelix; chlorins;  
15 chloroquinoxaline sulfonamide; cicaprost; cis-porphyrin; cladribine; clomifene analogues; clotrimazole; collismycin A; collismycin B; combretastatin A4; combretastatin analogue; conagenin; crambescidin 816; crisnatol; cryptophycin 8; cryptophycin A derivatives; curacin A; cyclopentantraquinones; cycloplatan; cypemycin; cytarabine ocfosfate; cytolytic factor; cytostatin; daclicximab; decitabine; dehydrodidemnin B; deslorelin; dexifosfamide;  
20 dexrazoxane; dexverapamil; diaziquone; didemnin B; didox; diethylnorspermine; dihydro-5-azacytidine; dihydrotaxol, 9-; dioxamycin; diphenyl spiromustine; discodermolide; docosanol; dolasetron; doxifluridine; droloxifene; dronabinol; duocarmycin SA; ebselen; ecomustine; edelfosine; edrecolomab; eflornithine; elemene; emitefur; epirubicin; epothilones including desoxyepothilones (A, R = H; B, R = Me); epithilones; epristeride; estramustine  
25 analogue; estrogen agonists; estrogen antagonists; etanidazole; etoposide; etoposide 4'-phosphate (etopofos); exemestane; fadrozole; fazarabine; fenretinide; filgrastim; finasteride; flavopiridol; flezelastine; fluasterone; fludarabine; fluorodaunorubicin hydrochloride; forfenimex; formestane; fostriecin; fotemustine; gadolinium texaphyrin; gallium nitrate; galocitabine; ganirelix; gelatinase inhibitors; gemcitabine; glutathione inhibitors; hepsulfam;  
30 heregulin; hexamethylene bisacetamide; hypericin; ibandronic acid; idarubicin; idoxifene; idramantone; ilmofosine; ilomastat; imidazoacridones; imiquimod; immunostimulant peptides; insulin-like growth factor-1 receptor inhibitor; interferon agonists; interferons; interleukins; iobenguane; iododoxorubicin; ipomeanol, 4-; irinotecan; iroplact; irsogladine;

isobengazole; isohomohalicondrin B; itasetron; jasplakinolide; kahalalide F; lamellarin-N triacetate; lanreotide; leinamycin; lenograstim; lentinan sulfate; leptolstatin; letrozole; leukemia inhibiting factor; leukocyte alpha interferon; leuprolide + estrogen + progesterone; leuprorelin; levamisole; liarozole; linear polyamine analogue; lipophilic disaccharide peptide; lipophilic platinum compounds; lissoclinamide 7; lobaplatin; lombricine; lometrexol; 5 lonidamine; losoxantrone; lovastatin; loxoribine; lurtotecan; lutetium texaphyrin; lysofylline; lytic peptides; maitansine; mannostatin A; marimastat; masoprocil; maspin; matrilysin inhibitors; matrix metalloproteinase inhibitors; menogaril; merbarone; meterelin; methioninase; metoclopramide; MIF inhibitor; mifepristone; miltefosine; mirimostim; mismatched double stranded RNA; mithracin; mitoguazone; mitolactol; mitomycin 10 analogues; mitonafide; mitotoxin fibroblast growth factor-saporin; mitoxantrone; mofarotene; molgramostim; monoclonal antibody, human chorionic gonadotrophin; monophosphoryl lipid A + myobacterium cell wall sk; mopidamol; multiple drug resistance gene inhibitor; multiple tumor suppressor 1-based therapy; mustard anticancer agent; mycaperoxide B; mycobacterial 15 cell wall extract; myriaporone; N-acetyldinaline; N-substituted benzamides; nafarelin; nagrestip; naloxone + pentazocine; napavin; naphterpin; nartograstim; nedaplatin; nemorubicin; neridronic acid; neutral endopeptidase; nilutamide; nisamycin; nitric oxide modulators; nitroxide antioxidant; nitrullin; O6-benzylguanine; octreotide; okicenone; oligonucleotides; onapristone; ondansetron; ondansetron; oracin; oral cytokine inducer; 20 ormaplatin; osaterone; oxaliplatin; oxaunomycin; paclitaxel analogues; paclitaxel derivatives; palauamine; palmitoylrhizoxin; pamidronic acid; panaxytriol; panomifene; parabactin; pazelliptine; pegaspargase; peldesine; pentosan polysulfate sodium; pentostatin; pentozole; perflubron; perfosfamide; perillyl alcohol; phenazinomycin; phenylacetate; phosphatase inhibitors; picibanil; pilocarpine hydrochloride; pirarubicin; piritrexim; placetin A; placetin B; 25 plasminogen activator inhibitor; platinum complex; platinum compounds; platinum-triamine complex; podophyllotoxin; porfimer sodium; porfiromycin; propyl bis-acridone; prostaglandin J2; proteasome inhibitors; protein A-based immune modulator; protein kinase C inhibitor; protein kinase C inhibitors, microalgal; protein tyrosine phosphatase inhibitors; purine nucleoside phosphorylase inhibitors; purpurins; pyrazoloacridine; pyridoxylated 30 hemoglobin polyoxyethylene conjugate; raf antagonists; raltitrexed; ramosetron; ras farnesyl protein transferase inhibitors; ras inhibitors; ras-GAP inhibitor; retelliptine demethylated; rhenium Re 186 etidronate; rhizoxin; ribozymes; RII retinamide; rogletimide; rohitukine; romurtide; roquinimex; rubiginone B1; ruboxyl; safingol; saintopin; SarCNU; sarcophytol A;

- 48 -

sargramostim; Sdi 1 mimetics; semustine; senescence derived inhibitor 1; sense oligonucleotides; signal transduction inhibitors; signal transduction modulators; single chain antigen binding protein; sizofiran; sobuzoxane; sodium borocaptate; sodium phenylacetate; solverol; somatomedin binding protein; sonermin; sparfosic acid; spicamycin D;

5 spiromustine; splenopentin; spongistatin 1; squalamine; stem cell inhibitor; stem-cell division inhibitors; stipiamide; stromelysin inhibitors; sulfinosine; superactive vasoactive intestinal peptide antagonist; suradista; suramin; swainsonine; synthetic glycosaminoglycans; tallimustine; tamoxifen methiodide; tauromustine; tazarotene; tecogalan sodium; tegafur; tellurapyrylium; telomerase inhibitors; temoporfin; temozolomide; teniposide;

10 tetrachlorodecaoxide; tetrazomine; thaliblastine; thalidomide; thiocoraline; thrombopoietin; thrombopoietin mimetic; thymalfasin; thymopoietin receptor agonist; thymotrinan; thyroid stimulating hormone; tin ethyl etiopurpurin; tirapazamine; titanocene dichloride; topotecan; topsentin; toremifene; totipotent stem cell factor; translation inhibitors; tretinoin; triacetyluridine; triciribine; trimetrexate; triptorelin; tropisetron; turosteride; tyrosine kinase

15 inhibitors; tyrphostins; UBC inhibitors; ubenimex; urogenital sinus-derived growth inhibitory factor; urokinase receptor antagonists; vapreotide; variolin B; vector system, erythrocyte gene therapy; velaresol; veramine; verdins; verteporfin; vinorelbine; vinxaltine; vitaxin; vorozole; zanoterone; zeniplatin; zilascorb; zinostatin stimalamer.

Anti-cancer Supplementary Potentiating Agents: Tricyclic anti-depressant drugs (e.g.,

20 imipramine, desipramine, amitriptyline, clomipramine, trimipramine, doxepin, nortriptyline, protriptyline, amoxapine and maprotiline); non-tricyclic anti-depressant drugs (e.g., sertraline, trazodone and citalopram);  $Ca^{++}$  antagonists (e.g., verapamil, nifedipine, nitrendipine and caroverine); Calmodulin inhibitors (e.g., prenylamine, trifluoroperazine and clomipramine); Amphotericin B; Triparanol analogues (e.g., tamoxifen); antiarrhythmic drugs (e.g.,

25 quinidine); antihypertensive drugs (e.g., reserpine); Thiol depleters (e.g., buthionine and sulfoximine) and Multiple Drug Resistance reducing agents such as Cremaphor EL. The compounds of the invention also can be administered with cytokines such as granulocyte colony stimulating factor.

Antiproliferative agent: Piritrexim Isethionate.

30 Radioactive agents: Fibrinogen I 125 ; Fludeoxyglucose F 18 ; Fluorodopa F 18 ; Insulin I 125; Insulin I 131; Iobenguane I 123; Iodipamide Sodium I 131 ; Iodoantipyrine I 131 ; Iodocholesterol I 131 ; Iodohippurate Sodium I 123 ; Iodohippurate Sodium I 125 ; Iodohippurate Sodium I 131 ; Iodopyracet I 125 ; Iodopyracet I 131 ; Iofetamine

- 49 -

Hydrochloride I 123 ; Iomethin I 125 ; Iomethin I 131 ; Iothalamate Sodium I 125 ;  
Iothalamate Sodium I 131 ; Iotyrosine I 131; Liothyronine I 125; Liothyronine I 131;  
Merisoprol Acetate Hg 197; Merisoprol Acetate Hg 203; Merisoprol Hg 197 ;  
Selenomethionine Se 75 ; Technetium Tc 99m Antimony Trisulfide Colloid; Technetium Tc  
5 99m Bicisate ; Technetium Tc 99m Disofenin ; Technetium Tc 99m Etidronate ; Technetium  
Tc 99m Exametazime ; Technetium Tc 99m Furifosmin ; Technetium Tc 99m Gluceptate ;  
Technetium Tc 99m Lidofenin ; Technetium Tc 99m Mebrofenin ; Technetium Tc 99m  
Medronate ; Technetium Tc 99m Medronate Disodium; Technetium Tc 99m Mertiatide ;  
Technetium Tc 99m Oxidronate ; Technetium Tc 99m Pentetate; Technetium Tc 99m  
10 Pentetate Calcium Trisodium; Technetium Tc 99m Sestamibi ; Technetium Tc 99m  
Siboroxime ; Technetium Tc 99m Succimer ; Technetium Tc 99m Sulfur Colloid ;  
Technetium Tc 99m Teboroxime ; Technetium Tc 99m Tetrofosmin ; Technetium Tc 99m  
Tiatide; Thyroxine I 125; Thyroxine I 131; Tolpovidone I 131 ; Triolein I 125; Triolein I 131.

The present invention further includes nucleic acid molecules formulated into a  
15 pharmaceutical composition for the inhibition of angiogenesis. The pharmaceutical  
compositions of the invention include those suitable for oral, rectal, nasal, topical (including  
buccal and sublingual), vaginal or parenteral (including subcutaneous, intramuscular,  
intravenous, intratumoral and intradermal) administration.

The nucleic acids are delivered in effective amounts. In general, the term "effective  
20 amount" of a nucleic acid refers to the amount necessary or sufficient to realize a desired  
biologic effect. Specifically, the effective amount is that amount that reduces the rate or  
inhibits altogether angiogenesis. For instance, when the subject bears a tumor having a blood  
supply, an effective amount is that amount which decreases or eliminates all together the  
blood supply to the tumor. Additionally, an effective amount may be that amount which  
25 prevents an increase or causes a decrease in new blood vessels, e.g., those vessels supplying a  
tumor. The effective amount may vary depending upon whether the antiangiogenic nucleic  
acid is used alone or in combination with other therapeutics, or in single or multiple dosages.  
In some instances, it is envisioned that the combination of antiangiogenic nucleic acids with  
other therapeutic agents (which are themselves not antiangiogenic nucleic acids) can result in  
30 a synergism between the two compound classes, and thereby would require less of one or both  
compounds in order to observe the desired biologic effect. Combined with the teachings  
provided herein, by choosing among the various active compounds and weighing factors such  
as potency, relative bioavailability, patient body weight, severity of adverse side-effects and

- 50 -

preferred mode of administration, an effective prophylactic or therapeutic treatment regimen can be planned which does not cause substantial toxicity and yet is entirely effective to treat the particular subject. As mentioned above, the effective amount for any particular application can vary depending on such factors as the type of condition having unwanted angiogenesis being treated or prevented, the particular nucleic acid being administered (e.g. the number of unmethylated CpG motifs or their location in the nucleic acid), the use of another antiangiogenesis agent, the size of the subject, or the severity of the disease or condition. One of ordinary skill in the art can empirically determine the effective amount of a particular nucleic acid molecule without necessitating undue experimentation.

Subject doses of the compounds described herein typically range from about 0.1  $\mu$ g to 10 mg per administration, which depending on the application could be given hourly, daily, weekly, or monthly and any other amount of time therebetween. More typically doses range from about 10  $\mu$ g to 5 mg per administration, and most typically from about 100  $\mu$ g to 1 mg, with 2 - 4 administrations being spaced hours, days or weeks apart. In some embodiments, however, parenteral doses for these purposes may be used in a range of 5 to 10,000 times higher than the typical doses described above.

For any compound described herein the therapeutically effective amount can be initially determined from animal models, e.g. the animal models described herein or those well known in the art. A therapeutically effective dose can also be determined from human data for CpG nucleic acids which have been tested in humans (human clinical trials have been initiated and the results publicly disseminated) and for compounds which are known to exhibit similar pharmacological activities, such as other antiangiogenesis agents. Higher doses may be required for parenteral administration, as described above. The applied dose can be adjusted based on the relative bioavailability and potency of the administered compound. Adjusting the dose to achieve maximal efficacy based on the methods described above and other methods as are well-known in the art is well within the capabilities of the ordinarily skilled artisan.

The formulations of the invention are administered in pharmaceutically acceptable solutions, which may routinely contain pharmaceutically acceptable concentrations of salt, buffering agents, preservatives, compatible carriers, adjuvants, and optionally other therapeutic ingredients.

For use in therapy, an effective amount of the nucleic acid can be administered to a subject by any mode that delivers the nucleic acid to a subject. "Administering" the

- 51 -

pharmaceutical composition of the present invention may be accomplished by any means known to the skilled artisan. Some routes of administration include but are not limited to oral, intranasal, intratracheal, inhalation, ocular, vaginal, rectal, parenteral (e.g. intramuscular, intradermal, intravenous, intratumoral or subcutaneous injection) and direct injection.

5 For oral administration, the compounds (i.e., antiangiogenic nucleic acid molecules and optionally other antiangiogenesis agents) can be delivered alone without any pharmaceutical carriers or formulated readily by combining the active compound(s) with pharmaceutically acceptable carriers well known in the art. The term "pharmaceutically-acceptable carrier" means one or more compatible solid or liquid filler, diluents or  
10 encapsulating substances which are suitable for administration to a human or other vertebrate animal. The term "carrier" denotes an organic or inorganic ingredient, natural or synthetic, with which the active ingredient is combined to facilitate the application. The components of the pharmaceutical compositions also are capable of being commingled with the compounds of the present invention, and with each other, in a manner such that there is no interaction  
15 which would substantially impair the desired pharmaceutical efficiency.

Such carriers enable the compounds of the invention to be formulated as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a subject to be treated. Pharmaceutical preparations for oral use can be obtained as solid excipient, optionally grinding a resulting mixture, and processing the mixture of granules,  
20 after adding suitable auxiliaries, if desired, to obtain tablets or dragee cores. Suitable excipients are, in particular, fillers such as sugars, including lactose, sucrose, mannitol, or sorbitol; cellulose preparations such as, for example, maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, and/or polyvinylpyrrolidone (PVP). If desired,  
25 disintegrating agents may be added, such as the cross-linked polyvinyl pyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate. Optionally the oral formulations may also be formulated in saline or buffers for neutralizing internal acid conditions.

Dragee cores may be provided with suitable coatings. For this purpose, concentrated sugar solutions may be used, which may optionally contain gum arabic, talc, polyvinyl  
30 pyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments may be added to the tablets or dragee coatings for identification or to characterize different combinations of active compound doses.



Pharmaceutical preparations which can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The push-fit capsules can contain the active ingredients in admixture with filler such as lactose, binders such as starches, and/or lubricants such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols. In addition, stabilizers may be added. Microspheres formulated for oral administration may also be used. Such microspheres have been well defined in the art. All formulations for oral administration should be in dosages suitable for such administration.

For buccal administration, the compositions may take the form of tablets or lozenges formulated in conventional manner.

For administration by inhalation, the compounds for use according to the present invention may be conveniently delivered in the form of an aerosol spray, from pressurized packs or a nebulizer, with the use of a suitable propellant, *e.g.*, dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas. In the case of a pressurized aerosol the dosage unit may be determined by providing a valve to deliver a metered amount. Capsules and cartridges of *e.g.* gelatin for use in an inhaler or insufflator may be formulated containing a powder mix of the compound and a suitable powder base such as lactose or starch.

The compounds, when it is desirable to deliver them systemically, may be formulated for parenteral administration by injection, *e.g.*, by bolus injection or continuous infusion. Formulations for injection may be presented in unit dosage form, *e.g.*, in ampoules or in multi-dose containers, with an added preservative. The compositions may take such forms as suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents.

Pharmaceutical formulations for parenteral administration include aqueous solutions of the active compounds in water-soluble form. Additionally, suspensions of the active compounds may be prepared as appropriate oily injection suspensions. Suitable lipophilic solvents or vehicles include fatty oils such as sesame oil, or synthetic fatty acid esters, such as ethyl oleate or triglycerides, or liposomes. Aqueous injection suspensions may contain substances which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Optionally, the suspension may also contain suitable stabilizers

- 53 -

or agents which increase the solubility of the compounds to allow for the preparation of highly concentrated solutions.

Alternatively, the active compounds may be in powder form for constitution with a suitable vehicle, *e.g.*, sterile pyrogen-free water, before use.

5       The compounds may also be formulated in rectal or vaginal compositions such as suppositories or retention enemas, *e.g.*, containing conventional suppository bases such as cocoa butter or other glycerides.

10       In addition to the formulations described previously, the compounds may also be formulated as a depot preparation. Such long acting formulations may be formulated with suitable polymeric or hydrophobic materials (for example as an emulsion in an acceptable oil) or ion exchange resins, or as sparingly soluble derivatives, for example, as a sparingly soluble salt.

15       The pharmaceutical compositions also may comprise suitable solid or gel phase carriers or excipients. Examples of such carriers or excipients include but are not limited to calcium carbonate, calcium phosphate, various sugars, starches, cellulose derivatives, gelatin, and polymers such as polyethylene glycols.

20       Suitable liquid or solid pharmaceutical preparation forms are, for example, aqueous or saline solutions for inhalation, microencapsulated, encochleated, coated onto microscopic gold particles, contained in liposomes, nebulized, aerosols, pellets for implantation into the skin, or dried onto a sharp object to be scratched into the skin. The pharmaceutical compositions may also include granules, powders, tablets, coated tablets, (micro)capsules, suppositories, syrups, emulsions, suspensions, creams, drops or preparations with protracted release of active compounds, in whose preparation excipients and additives and/or auxiliaries such as disintegrants, binders, coating agents, swelling agents, lubricants, flavorings, 25       sweeteners or solubilizers are customarily used as described above. The pharmaceutical compositions are suitable for use in a variety of drug delivery systems. For a brief review of present methods for drug delivery, see Langer, *Science* 249:1527-1533, 1990, which is incorporated herein by reference.

30       The nucleic acid molecules and/or agents (*e.g.*, antiangiogenesis agents, anticancer agents) may be administered per se (neat) or in the form of a pharmaceutically acceptable salt. When used in medicine the salts should be pharmaceutically acceptable, but non-pharmaceutically acceptable salts may conveniently be used to prepare pharmaceutically acceptable salts thereof. Such salts include, but are not limited to, those prepared from the

following acids: hydrochloric, hydrobromic, sulphuric, nitric, phosphoric, maleic, acetic, salicylic, p-toluene sulphonic, tartaric, citric, methane sulphonic, formic, malonic, succinic, naphthalene-2-sulphonic, and benzene sulphonic. Also, such salts can be prepared as alkaline metal or alkaline earth salts, such as sodium, potassium or calcium salts of the carboxylic acid group.

Suitable buffering agents include: acetic acid and a salt (1-2% w/v); citric acid and a salt (1-3% w/v); boric acid and a salt (0.5-2.5% w/v); and phosphoric acid and a salt (0.8-2% w/v). Suitable preservatives include benzalkonium chloride (0.003-0.03% w/v); chlorobutanol (0.3-0.9% w/v); parabens (0.01-0.25% w/v) and thimerosal (0.004-0.02% w/v).

The nucleic acids or other therapeutics useful in the invention may be delivered in mixtures with additional antiangiogenesis agent(s). A mixture may consist of several antiangiogenesis agents in addition to the nucleic acid.

A variety of administration routes are available. The particular mode selected will depend, of course, upon the particular nucleic acid molecules or other agents selected, the particular condition being treated and the dosage required for therapeutic efficacy. The methods of this invention, generally speaking, may be practiced using any mode of administration that is medically acceptable, meaning any mode that produces effective levels of an immune response without causing clinically unacceptable adverse effects. Preferred modes of administration are discussed above.

The compositions may conveniently be presented in unit dosage form and may be prepared by any of the methods well known in the art of pharmacy. All methods include the step of bringing the compounds into association with a carrier which constitutes one or more accessory ingredients. In general, the compositions are prepared by uniformly and intimately bringing the compounds into association with a liquid carrier, a finely divided solid carrier, or both, and then, if necessary, shaping the product. Liquid dose units are vials or ampoules. Solid dose units are tablets, capsules and suppositories.

Other delivery systems can include time-release, delayed release or sustained release delivery systems. Such systems can avoid repeated administrations of the compounds, increasing convenience to the subject and the physician. Many types of release delivery systems are available and known to those of ordinary skill in the art. They include polymer base systems such as poly(lactide-glycolide), copolyoxalates, polycaprolactones, polyesteramides, polyorthoesters, polyhydroxybutyric acid, and polyanhydrides. Microcapsules of the foregoing polymers containing drugs are described in, for example, U.S.

- 55 -

Patent 5,075,109. Delivery systems also include non-polymer systems that are: lipids including sterols such as cholesterol, cholesterol esters and fatty acids or neutral fats such as mono-di-and tri-glycerides; hydrogel release systems; sylastic systems; peptide based systems; wax coatings; compressed tablets using conventional binders and excipients; partially fused implants; and the like. Specific examples include, but are not limited to: (a) erosional systems in which an agent of the invention is contained in a form within a matrix such as those described in U.S. Patent Nos. 4,452,775, 4,675,189, and 5,736,152, and (b) diffusional systems in which an active component permeates at a controlled rate from a polymer such as described in U.S. Patent Nos. 3,854,480, 5,133,974 and 5,407,686. In addition, pump-based hardware delivery systems can be used, some of which are adapted for implantation. In still other embodiments, the agents and nucleic acids are formulated with GELFOAM, a commercial product consisting of modified collagen fibers that degrade slowly.

The nucleic acid may be directly administered to the subject or may be administered in conjunction with a pharmaceutically acceptable carrier or a delivery vehicle. The nucleic acid and optionally other therapeutic agents may be administered alone (e.g. in saline or buffer) or using any delivery vehicles known in the art. One type of delivery vehicle is referred to herein as a nucleic acid delivery complex. A "nucleic acid delivery complex" shall mean a nucleic acid molecule associated with (e.g. ionically or covalently bound to; or encapsulated within) a targeting means (e.g. a molecule that results in higher affinity binding to target cell (e.g. dendritic cell surfaces and/or increased cellular uptake by target cells). Examples of nucleic acid delivery complexes include nucleic acids associated with: a sterol (e.g. cholesterol), a lipid (e.g. a cationic lipid, virosome or liposome), or a target cell specific binding agent (e.g. a ligand recognized by target cell specific receptor). Preferred complexes may be sufficiently stable *in vivo* to reduce significant uncoupling prior to internalization by the target cell. However, the complex may be cleavable under appropriate conditions within the cell so that the nucleic acid may be released in a functional form.

The nucleic acid molecules may be delivered by non-invasive methods as described above. Non-invasive delivery of compounds is desirable for treatment of children, elderly, animals, and even adults and also to avoid the risk of needle-stick injury. Delivery vehicles for delivering compounds to mucosal surfaces have been described and include but are not limited to: cochleates, emulsomes, ISCOMs, liposomes, live bacterial vectors (e.g., *Salmonella*, *Escherichia coli*, *Bacillus calmatte-guerin*, *Shigella*, *Lactobacillus*), live viral vectors (e.g., Vaccinia, adenovirus, Herpes Simplex), microspheres, nucleic acid vaccines,

polymers (e.g. carboxymethylcellulose, chitosan), polymer rings, proteosomes, sodium fluoride, transgenic plants, virosomes, and virus-like particles.

### Examples

#### 1. Background

##### *1.1. Angiogenesis*

Angiogenesis describes the active biological process of blood vessel formation from pre-existing microvasculature (1, 2). In multi-celled organisms this is a highly organized and tightly regulated process that occurs normally during development, inflammation, and tissue repair. The importance of angiogenesis is reflected in the need of mammalian cells for oxygen and nutrients. Mammalian cells must be within a 200  $\mu$ M distance of blood vessels, which is the diffusion limit for oxygen (3). Thus the overall driving factor for angiogenesis is the requirement for oxygen and nutrients. The normal regulation of angiogenesis is mediated by the balance between pro- and anti-angiogenic factors that are released in the tissues and are influenced by local environmental factors.

##### *1.2. Angiogenesis and neoplasms*

In a neoplastic situation, the balances of these pro- and anti-angiogenic factors are generally skewed in favor of angiogenesis. In this setting, angiogenesis is generally a highly disorganized and loosely regulated process that is an absolute requirement for the continued growth of neoplasms (3). Further, there is a direct correlation between the extent of vascularization found in neoplasms and the potential for metastasis (4).

##### *1.3. Angiogenesis and chemokines*

There are a number of pro- and anti-angiogenic factors that have been described to date (3). The focus of this analysis will be on the chemokines interferon- $\gamma$ -inducible protein (IP-10) and monokine induced by interferon- $\gamma$  (MIG). Chemokines are a collection of cytokines that possess chemoattracting properties (for review see (5)). Chemokines are classified on the basis of the motif displayed by the first two cysteine residues present in the protein (CXC, CC, C, or CX3C), and they signal through G-protein coupled, seven-transmembrane receptors. Initially identified for their influence on hemopoietic cell migration, chemokines are now known to influence a number of physiological and pathological process including angiogenesis and angiostasis (5).

- 57 -

IP-10 and MIG belong to a subset of the family of CXC chemokines (2) that bind the chemokine receptor CXCR3 (6). The CXC chemokine family can be further subdivided based on the presence or absence of a Glu-Leu-Arg or ELR motif at the NH<sub>2</sub> terminus of the chemokine. CXC chemokines that contain the ELR motif are potent promoters of angiogenesis whereas CXC chemokines that lack the ELR motif, as is the case for IP-10 and MIG, are potent inhibitors of angiogenesis (2).

## 2. Material and Methods

### 2.1. ODNs

10 ODN 1826 (TCCATGACGTTTCCTGACGTT; SEQ ID NO: 69)

### 2.2 Matrigel® - (BD)

Matrix solution is liquid at 4°C and solidifies at room temperature. When injected *in vivo* Matrigel solidifies to form a plug. Matrigel allows for the delivery of angiogenic promoters such as basic fibroblastic growth factor (bFGF) for the induction of angiogenesis. Plugs can  
15 then be removed to evaluate the level of angiogenesis as identified by the concentration of hemoglobin present. This system can be used to evaluate the anti-angiogenic potential of different compounds.

### 2.3 Hemoglobin quantification kit

Drabkin method reagent kit (Sigma)

### 20 2.4 Protein quantification

Protein quantification kit (BioRad)

### 2.5 Experimental design

For each group of 5 mice, the Matrigel was prepared as follows:

#### Group 1 - Matrigel alone.

25 3.5 mL of Matrigel

500 µL/mouse was injected subcutaneously (SC) right of center of the abdomen

#### Group 2 - Matrigel + bFGF (150ng/mL) + heparin (40 units/mL)

52.5 µL bFGF (10µg/mL)

23.2 µL heparin (6039 units/mL)

30 3.42 mL Matrigel

500 µL/mouse was injected SC right of center of the abdomen

#### Group 3 - Matrigel + bFGF (150 ng/mL) + heparin (40 units/mL) + oligo 1826 (1mg/mL)

- 58 -

52.5  $\mu$ L bFGF (10 $\mu$ g/mL)

23.2  $\mu$ L heparin (6039 units/mL)

233  $\mu$ L oligo 1826 (15mg/mL)

3.19 mL Matrigel

5 500 $\mu$ L/mouse was injected SC right of center of the abdomen

Group 4 - Matrigel + bFGF (150ng/mL) + heparin (40 units/mL)

52.5  $\mu$ L bFGF (10 $\mu$ g/mL)

23.2  $\mu$ L heparin (6039 units/mL)

3.42 mL Matrigel

10 500  $\mu$ L/mouse was injected SC right of center of the abdomen

This group received daily SC injections, for 6 days, of 100  $\mu$ L of ODN 1826 (1mg/mL) on the opposite flank from the Matrigel plug.

### ***2.6 Determination of Hemoglobin and total protein content of Matrigel plugs***

On day 6 the animals were euthanised and the Matrigel plugs collected. The plugs were  
15 placed in 0.3 mL of sterile PBS and placed at 4°C over night to allow the Matrigel to liquify.  
The hemoglobin and total protein content of the Matrigel plugs was determined using the  
methods described above. The hemoglobin content of the Matrigel plugs was expressed as  
(mg/mL)/mg of total protein.

## **20 3. Preliminary Results**

When angiogenic factors were added to the Matrigel (Group 2), there was a significant  
increase in the amount of hemoglobin present in the Matrigel plug at 6 days when compared  
to Matrigel alone (Group 1) ( $p < 0.05$ ). (See Figure 1.)

When CpG was included in the Matrigel plug along with the angiogenic factors  
25 (Group 3), there was a greater than 2 fold decrease in the amount of hemoglobin present in the  
Matrigel plug at 6 days when compared to the Matrigel containing the angiogenic factors  
(Group 2). (See Figure 1.)

When CpG was administered daily by subcutaneous injection, rather than present in  
the Matrigel plug, to the mouse in the flank opposite to the Matrigel plug which contained  
30 angiogenic factors (Group 4) there was no significant difference in the amount of hemoglobin  
present in the Matrigel plug at 6 days when compared to Matrigel containing the angiogenic  
factors (Group 2). (See Figure 1.)

- 59 -

These preliminary results suggest that the inclusion of CpG ODN directly within the Matrigel (Group 3) had a negative influence on angiogenesis. Although daily delivery of CpG to the opposite flank from the Matrigel plug did not appear to influence angiogenesis, it is possible that CpG administered intravenously or subcutaneously in a region closer to the plug (and accordingly tumor mass) would manifest anti-angiogenic activity. CpG ODN may have to be present in the vicinity of active angiogenesis in order to have a negative influence.

#### 4. References

1. Carmeliet, P. 2000. Mechanisms of angiogenesis and arteriogenesis. *Nat Med.* 6: 389-95.
- 10 2. Belperio, J. A., et al. 2000. CXC chemokines in angiogenesis. *J Leukoc Biol.* 68: 1-8.
3. Carmeliet, P., R. K. Jain. 2000. Angiogenesis in cancer and other diseases. *Nature.* 407: 249-57.
4. Zetter, B. R. 1998. Angiogenesis and tumor metastasis. *Annu Rev Med.* 49: 407-24.
5. Rossi, D., A. Zlotnik. 2000. The biology of chemokines and their receptors. *Annu Rev*
- 15 *Immun.* 18: 217-42.
6. Loetscher, M., et al. 1996. Chemokine receptor specific for IP10 and MIG: structure, function, and expression in activated T-lymphocytes. *J Exp Med.* 184: 963-9.
7. Coughlin, C. M., et al. 1998. Tumor cell responses to IFNgamma affect tumorigenicity and response to IL-12 therapy and antiangiogenesis. *Immunity.* 9: 25-34.
- 20 8. Strasly, M., et al. 2001. IL-12 inhibition of endothelial cell functions and angiogenesis depends on lymphocyte-endothelial cell cross-talk. *J Immunol.* 166: 3890-9.
9. Kanegane, C., et al. 1998. Contribution of the CXC chemokines IP-10 and Mig to the antitumor effects of IL-12. *J Leukoc Biol.* 64: 384-92.

#### Equivalents

It should be understood that the preceding is merely a detailed description of certain preferred embodiments. It therefore should be apparent to those of ordinary skill in the art that various modifications and equivalents can be made without departing from the spirit and scope of the invention. It is intended that the invention encompass all such modifications within the scope of the appended claims. All references, patents and patent applications and publications that are cited or referred to in this application are incorporated in their entirety herein by reference.



I claim:

- 61 -

Claims

1. A method of inhibiting angiogenesis in a subject in need of such treatment comprising administering to the subject at least one antiangiogenic nucleic acid molecule in an amount effective to inhibit angiogenesis in the subject.  
5
2. The method of claim 1, wherein the at least one antiangiogenic nucleic acid molecule comprises at least one sequence set forth as SEQ ID NOs: 1-1093.
3. The method of claim 1, wherein two or more antiangiogenic nucleic acid molecules  
10 are administered.
4. The method of claim 1, further comprising administering to the subject at least one non-nucleic acid angiogenesis inhibitor molecule.
- 15 5. The method of claim 1, wherein the angiogenesis is associated with a condition selected from the group consisting of a solid tumor growth, a tumor metastasis, and a precancerous lesion.
6. The method of claim 1, wherein the nucleic acid is a CpG nucleic acid having an  
20 unmethylated CpG motif.
7. The method of claim 1, wherein the nucleic acid is a T-rich nucleic acid.
8. The method of claim 1, wherein the nucleic acid is a poly G nucleic acid.  
25
9. The method of claim 1, wherein the nucleic acid is isolated.
10. The method of claim 1, wherein the nucleic acid does not encode a protein having  
antiangiogenesis activity.  
30
11. The method of claim 1, wherein the nucleic acid has a modified backbone.

- 62 -

12. The method of claim 11, wherein the modified backbone is a phosphate backbone modification.
13. The method of claim 11, wherein the modified backbone is a peptide modified  
5 oligonucleotide backbone.
14. The method of claim 1, further comprising administering to the subject at least one anticancer agent.
- 10 15. The method of claim 1, further comprising administering to the subject at least one antiarthritis agent.
16. The method of claim 6, wherein the CpG nucleic acid comprises:  
$$5' X_1 X_2 CGX_3 X_4 3'$$
  
15 wherein C is unmethylated, and wherein  $X_1X_2$  and  $X_3X_4$  are nucleotides.
17. The method of claim 16, wherein the  $5' X_1 X_2 CGX_3 X_4 3'$  sequence is a non-palindromic sequence.
- 20 18. The method of claim 16, wherein the CpG nucleic acid has 8 to 100 nucleotides.
19. The method of claim 16, wherein  $X_1X_2$  are nucleotides selected from the group consisting of: GpT, GpG, GpA, ApA, ApT, ApG, CpT, CpA, CpG, TpA, TpT, and TpG; and  $X_3X_4$  are nucleotides selected from the group consisting of: TpT, CpT, ApT, TpG, ApG, CpG,  
25 TpC, ApC, CpC, TpA, ApA, and CpA.
20. The method of claim 16, wherein  $X_1X_2$  are selected from the group consisting of GpA and GpT and  $X_3X_4$  are TpT.
- 30 21. The method of claim 16, wherein  $X_1X_2$  are both purines and  $X_3X_4$  are both pyrimidines.
22. The method of claim 16, wherein  $X_2$  is a T and  $X_3$  is a pyrimidine.

- 63 -

23. The method of claim 16, wherein the CpG nucleic acid is 8 to 40 nucleotides in length.

24. The method of claim 16, wherein the CpG nucleic acid has a sequence selected from  
5 the group consisting of SEQ ID NOs: 1, 3, 4, 14-16, 18-24, 28, 29, 33-46, 49, 50, 52-56, 58,  
64-67, 69, 71, 72, 76-87, 90, 91, 93, 94, 96, 98, 102-124, 126-128, 131-133, 136-141, 146-  
150, 152-153, 155-171, 173-178, 180-186, 188-198, 201, 203-214, 216-220, 223, 224, 227-  
240, 242-256, 258, 260-265, 270-273, 275, 277-281, 286-287, 292, 295-296, 300, 302, 305-  
307, 309-312, 314-317, 320-327, 329, 335, 337-341, 343-352, 354, 357, 361-365, 367-369,  
10 373-376, 378-385, 388-392, 394, 395, 399, 401-404, 406-426, 429-433, 434-437, 439, 441-  
443, 445, 447, 448, 450, 453-456, 460-464, 466-469, 472-475, 477, 478, 480, 483-485, 488,  
489, 492, 493, 495-502, 504-505, 507-509, 511, 513-529, 532-541, 543-555, 564-566, 568-  
576, 578, 580, 599, 601-605, 607-611, 613-615, 617, 619-622, 625-646, 648-650, 653-664,  
666-697, 699-706, 708, 709, 711-716, 718-732, 736, 737, 739-744, 746, 747, 749-761, 763,  
15 766-767, 769, 772-779, 781-783, 785-786, 7900792, 798-799, 804-808, 810, 815, 817, 818,  
820-832, 835-846, 849-850, 855-859, 862, 865, 872, 874-877, 879-881, 883-885, 888-904,  
and 909-913.

25. The method of claim 7, wherein the T-rich nucleic acid is a poly T nucleic acid  
20 comprising

5' TTTT 3'.

26. The method of claim 25, wherein the poly T nucleic acid comprises

5' X<sub>1</sub> X<sub>2</sub> TTTT X<sub>3</sub> X<sub>4</sub> 3'

25 wherein X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub> and X<sub>4</sub> are nucleotides.

27. The method of claim 25, wherein the T rich nucleic acid comprises a plurality of poly  
T nucleic acid motifs.

30 28. The method of claim 26, wherein X<sub>1</sub>X<sub>2</sub> is TT.

29. The method of claim 26, wherein X<sub>3</sub>X<sub>4</sub> is TT.

- 64 -

30. The method of claim 26, wherein  $X_1X_2$  is selected from the group consisting of TA, TG, TC, AT, AA, AG, AC, CT, CC, CA, CG, GT, GG, GA, and GC.
31. The method of claim 26, wherein  $X_3X_4$  is selected from the group consisting of TA,  
5 TG, TC, AT, AA, AG, AC, CT, CC, CA, CG, GT, GG, GA, and GC.
32. The method of claim 25, wherein the T rich nucleic acid comprises a nucleotide composition of greater than 25% T.
- 10 33. The method of claim 7, wherein the T rich nucleic acid comprises a nucleotide composition of greater than 25% T.
34. The method of claim 33, wherein the T rich nucleic acid comprises a nucleotide composition of greater than 30% T.
- 15 35. The method of claim 33, wherein the T rich nucleic acid comprises a nucleotide composition of greater than 50% T.
36. The method of claim 33, wherein the T rich nucleic acid comprises a nucleotide  
20 composition of greater than 60% T.
37. The method of claim 33, wherein the T rich nucleic acid comprises a nucleotide composition of greater than 80% T.
- 25 38. The method of claim 7, wherein the T rich nucleic acid comprises at least 20 nucleotides.
39. The method of claim 7, wherein the T rich nucleic acid comprises at least 24 nucleotides.
- 30 40. The method of claim 8, wherein the poly G nucleic acid comprises:  
$$5' X_1X_2GGGX_3X_4 3'$$
  
wherein  $X_1$ ,  $X_2$ ,  $X_3$ , and  $X_4$  are nucleotides.

- 65 -

41. The method of claim 40, wherein at least one of X<sub>3</sub> and X<sub>4</sub> are a G.

42. The method of claim 40, wherein both of X<sub>3</sub> and X<sub>4</sub> are a G.

43. The method of claim 8, wherein the poly G nucleic acid comprises the following formula:



wherein N represents between 0 and 20 nucleotides.

44. The method of claim 8, wherein the poly G nucleic acid comprises the following formula:



wherein N represents between 0 and 20 nucleotides.

45. The method of claim 8, wherein the poly G nucleic acid is free of unmethylated CG dinucleotides

46. The method of claim 45, wherein the poly G nucleic acid is selected from the group consisting of SEQ ID NOs: 5, 6, 73, 215, 267-269, 276, 282, 288, 297-299, 355, 359, 386, 387, 444, 476, 531, 557-559, 733, 768, 795, 796, 914-925, 928-931, 933-936, and 938.

47. The method of claim 8, wherein the poly G nucleic acid includes at least one unmethylated CG dinucleotide.

48. The method of claim 47, wherein the poly G nucleic acid is selected from the group consisting of SEQ ID NOs: 67, 80-82, 141, 147, 148, 173, 178, 183, 185, 214, 224, 264, 265, 315, 329, 434, 435, 475, 519, 521-524, 526, 527, 535, 554, 565, 609, 628, 660, 661, 662, 725, 767, 825, 856, 857, 876, 892, 909, 926, 927, 932, and 937.

49. The method of claim 1, wherein the nucleic acid is a synthetic nucleic acid.

50. The method of claim 9, wherein the nucleic acid is administered on a routine schedule.

- 66 -

51. The method of claim 1, wherein the angiogenesis is associated with a condition selected from the group consisting of rheumatoid arthritis, psoriasis, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, Osler-Webber Syndrome, myocardial angiogenesis, plaque neovascularization, telangiectasia, hemophiliac joints, angiofibroma, wound granulation, intestinal adhesions, atherosclerosis, scleroderma, and hypertrophic scars.
52. The method of claim 1, wherein the nucleic acid is not an antisense molecule.
53. A pharmaceutical composition comprising an amount of at least one antiangiogenic nucleic acid molecule effective to inhibit angiogenesis and a pharmaceutically acceptable carrier.
54. The pharmaceutical composition of claim 53, wherein the at least one antiangiogenic nucleic acid molecule comprises at least one sequence set forth as SEQ ID NOs: 1-1093.
55. The pharmaceutical composition of claim 53, wherein two or more antiangiogenic nucleic acid molecules are administered.
56. The pharmaceutical composition of claim 53, further comprising at least one non-nucleic acid angiogenesis inhibitor molecule.
57. The pharmaceutical composition of claim 53, wherein the antiangiogenic nucleic acid molecule has a modified backbone.
58. The pharmaceutical composition of claim 57, wherein the modified backbone is a phosphate modified backbone.
59. The pharmaceutical composition of claim 58, wherein the phosphate modified backbone is a phosphorothioate modified backbone.
60. The pharmaceutical composition of claim 53, further comprising an anticancer agent.

- 67 -

61. The pharmaceutical composition of claim 53, wherein the nucleic acid is a CpG nucleic acid.
- 5 62. The pharmaceutical composition of claim 53, wherein the nucleic acid is a T-rich nucleic acid.
63. The pharmaceutical composition of claim 53, wherein the nucleic acid is a poly G nucleic acid.
- 10 64. The pharmaceutical composition of claim 53, wherein the nucleic acid is isolated.
65. The pharmaceutical composition of claim 53, wherein the nucleic acid is not an antisense molecule.
- 15 66. A kit comprising  
a first container housing at least one antiangiogenic nucleic acid molecule, and  
instructions for administering the antiangiogenic nucleic acid to a subject having a condition characterized by unwanted angiogenesis.
- 20 67. The kit of claim 66, wherein the antiangiogenic nucleic acid has a modified backbone.
68. The kit of claim 67, wherein the modified backbone is a phosphate modified backbone.
- 25 69. The kit of claim 67, wherein the phosphate modified backbone is a phosphorothioate modified backbone.
70. The kit of claim 65, further comprising a second container housing at least one non-nucleic acid antiangiogenic agent.
- 30 71. The kit of claim 65, further comprising a second container housing at least one anticancer agent.



- 68 -

72. The kit of claim 69, further comprising a third container housing at least one anticancer agent.

5 73. The kit of claim 65, wherein the nucleic acid is not an antisense molecule.

74. The kit of claim 65, wherein the instructions relate to administering the antiangiogenic nucleic acid to a subject having a condition selected from the group consisting of rheumatoid arthritis, psoriasis, diabetic retinopathy, retinopathy of prematurity, macular degeneration,  
10 corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, Osler-Webber Syndrome, myocardial angiogenesis, plaque neovascularization, telangiectasia, hemophiliac joints, angiofibroma, wound granulation, intestinal adhesions, atherosclerosis, scleroderma, and hypertrophic scars.

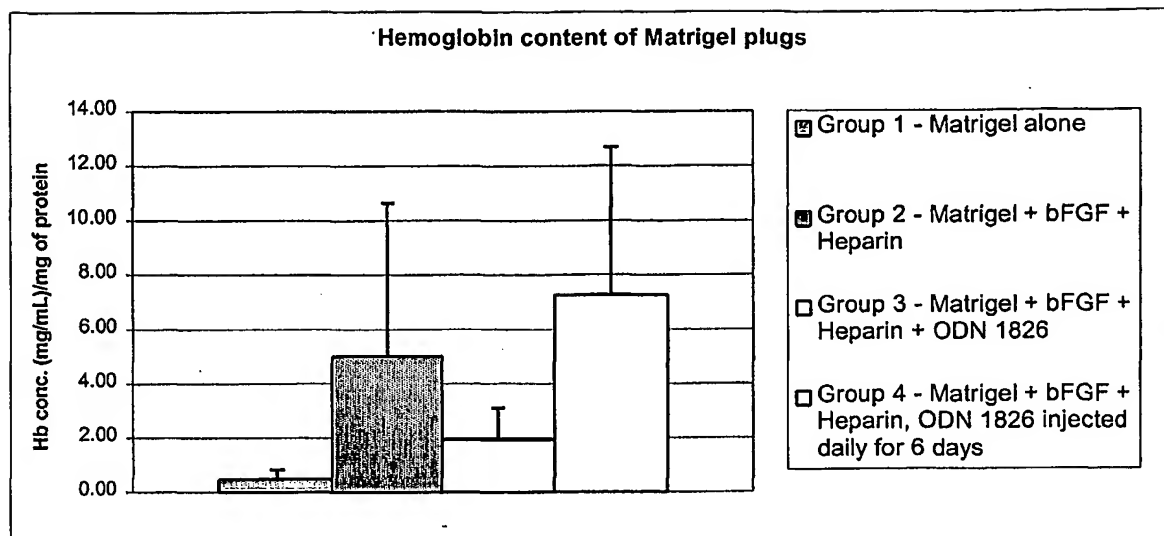


Figure 1

- 1 -

## SEQUENCE LISTING

&lt;110&gt; Coley Pharmaceutical Group, Inc.

&lt;120&gt; Inhibition of Angiogenesis by Nucleic Acids

&lt;130&gt; C1037/7025WO (HCL/MAT)

&lt;150&gt; US 60/255,534

&lt;151&gt; 2000-12-14

&lt;160&gt; 1093

&lt;170&gt; FastSEQ for Windows Version 3.0

&lt;210&gt; 1

&lt;211&gt; 18

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 1

tctcccagcg tgcgccat

18

&lt;210&gt; 2

&lt;211&gt; 20

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 2

ataatocagc ttgaaccaag

20

&lt;210&gt; 3

&lt;211&gt; 20

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 3

ataatcgacg ttcaagcaag

20

&lt;210&gt; 4

&lt;211&gt; 18

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 4

taccggtgc gaccctct

18

- 2 -

<210> 5  
<211> 9  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 5  
ggggagggt 9  
  
<210> 6  
<211> 9  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 6  
ggggagggg 9  
  
<210> 7  
<211> 9  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 7  
ggtgagggtg 9  
  
<210> 8  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<221> modified\_base  
<222> (8)...(8)  
<223> m5c  
  
<223> Synthetic Sequence  
  
<400> 8  
tccatgtngt tcctgatgct 20  
  
<210> 9  
<211> 15  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<221> modified\_base  
<222> (11)...(11)  
<223> m5c  
  
<223> Synthetic Sequence

<400> 9  
gctaccttag ngtga 15

<210> 10  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (8)...(8)  
<223> m5c

<223> Synthetic Sequence

<400> 10  
tccatgangt tctgatgct 20

<210> 11  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (13)...(13)  
<223> m5c

<223> Synthetic Sequence

<400> 11  
tccatgacgt tcntgatgct 20

<210> 12  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (7)...(7)  
<223> m5c

<223> Synthetic Sequence

<400> 12  
gctagangtt agtgt 15

<210> 13  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 13  
agctccatgg tgctcactg 19

<210> 14  
<211> 20

- 4 -

<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 14  
ccacgtcgac cctcaggcga 20

<210> 15  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 15  
gcacatcgtc ccgcagccga 20

<210> 16  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 16  
gtcactcgtg gtacctcga 19

<210> 17  
<211> 25  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 17  
gttggataca ggccagactt tgttg 25

<210> 18  
<211> 25  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 18  
gattcaactt gcgctcatct taggc 25

<210> 19  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 19  
accatggacg aactgtttcc cctc 24

<210> 20  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 20  
accatggacg agctgtttcc cctc 24

<210> 21  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 21  
accatggacg acctgtttcc cctc 24

<210> 22  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 22  
accatggacg tactgtttcc cctc 24

<210> 23  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 23  
accatggacg gtctgtttcc cctc 24

<210> 24  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 24  
accatggacg ttctgtttcc cctc 24

<210> 25  
<211> 25  
<212> DNA

<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 25  
ccactcacat ctgctgctcc acaag 25

<210> 26  
<211> 25  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 26  
acttctcata gtccctttgg tccag 25

<210> 27  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 27  
tccatgagct tcctgagtct 20

<210> 28  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<221> modified\_base  
<222> (9)...(9)  
<223> I

<221> modified\_base  
<222> (11)...(11)  
<223> I

<221> modified\_base  
<222> (15)...(15)  
<223> I

<400> 28  
gaggaaggng nggangacgt 20

<210> 29  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence



- 7 -

<221> modified\_base  
<222> (7)...(7)  
<223> I

<221> modified\_base  
<222> (13)...(13)  
<223> I

<221> modified\_base  
<222> (18)...(18)  
<223> I

<400> 29  
gtgaatncgt tcncgggnct 20

<210> 30  
<211> 6  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 30  
aaaaaa 6

<210> 31  
<211> 6  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 31  
cccccc 6

<210> 32  
<211> 6  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 32  
ctgtca 6

<210> 33  
<211> 6  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 33  
tcgtag 6

<210> 34  
<211> 6

- 8 -

<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 34  
tcgtgg 6  
  
<210> 35  
<211> 6  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 35  
cgtcgt 6  
  
<210> 36  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 36  
tccatgtcgg tcctgagtct 20  
  
<210> 37  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 37  
tccatgccgg tcctgagtct 20  
  
<210> 38  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 38  
tccatgacgg tcctgagtct 20  
  
<210> 39  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence

<400> 39  
tccatgacgg tcctgagtct 20

<210> 40  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 40  
tccatgtcga tcctgagtct 20

<210> 41  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 41  
tccatgtcgc tcctgagtct 20

<210> 42  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 42  
tccatgtcgt tcctgagtct 20

<210> 43  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 43  
tccatgacgt tcctgagtct 20

<210> 44  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 44  
tccataacgt tcctgagtct 20

<210> 45  
<211> 20  
<212> DNA

- 10 -

<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 45  
tccatgacgt ccctgagtct 20

<210> 46  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 46  
tccatcacgt gcctgagtct 20

<210> 47  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 47  
tccatgctgg tcctgagtct 20

<210> 48  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (8)...(8)  
<223> m5c

<223> Synthetic Sequence

<400> 48  
tccatgtngg tcctgagtct 20

<210> 49  
<211> 39  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 49  
ccgcttcctc cagatgagct catgggtttc tccaccaag 39

<210> 50  
<211> 39  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 50  
cttggtggag aaacccatga gctcatctgg aggaagcgg 39

<210> 51  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 51  
ccccaagg atgagaagtt 20

<210> 52  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 52  
agatagcaaa tcggctgacg 20

<210> 53  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 53  
ggttcacgtg ctcattggctg 20

<210> 54  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 54  
tctcccagcg tgcgccat 18

<210> 55  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 55  
tctcccagcg tgcgccat 18

- 12 -

<210> 56  
<211> 18  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 56  
taccgcgtgc gaccctct 18  
  
<210> 57  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 57  
ataatccagc ttgaaccaag 20  
  
<210> 58  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 58  
ataatcgacg ttcaagcaag 20  
  
<210> 59  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 59  
tccatgattt tcctgatttt 20  
  
<210> 60  
<211> 24  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 60  
ttgttttttt gttttttgt tttt 24  
  
<210> 61  
<211> 22  
<212> DNA  
<213> Artificial Sequence  
  
<220>

- 13 -

<223> Synthetic Sequence

<400> 61  
ttttttttgt ttttttgttt tt 22

<210> 62  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 62  
tgctgctttt gtgcttttgc gctt 24

<210> 63  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 63  
tgctgcttgc gcttttgc tt 22

<210> 64  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 64  
gcattcatca ggcgggcaag aat 23

<210> 65  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 65  
taccgagctt cgacgagatt tca 23

<210> 66  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 66  
gcatgacgctt gagct 15

<210> 67

- 14 -

<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 67  
cacgttgagg ggcac 15

<210> 68  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 68  
ctgctgagac tggag 15

<210> 69  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 69  
tccatgacgt tcctgacgtt 20

<210> 70  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 70  
gcatgagctt gagctga 17

<210> 71  
<211> 12  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 71  
tcagcgtgcg cc 12

<210> 72  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence



<400> 72  
atgacgttcc tgacgtt 17

<210> 73  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 73  
ttttgggggtt ttgggggttt 20

<210> 74  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 74  
tctaggcttt ttaggcttcc 20

<210> 75  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 75  
tgcatttttt aggccacat 20

<210> 76  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 76  
tctcccagcg tgcgtgcgcc at 22

<210> 77  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 77  
tctcccagcg ggcgcat 17

<210> 78  
<211> 18

<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 78  
tctcccagcg agcgccat 18

<210> 79  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 79  
tctcccagcg cgcgccat 18

<210> 80  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 80  
ggggtgacgt tcagggggg 19

<210> 81  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 81  
ggggtccagc gtgcgccatg gggg 24

<210> 82  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 82  
ggggtgtcgt tcagggggg 19

<210> 83  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 83  
tccatgtcgt tcctgtcggt 20

<210> 84  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 84  
tccatagcgt tccatagcgt 20

<210> 85  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 85  
tcgtcgtgt ctccgcttct t 21

<210> 86  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 86  
gcatgacgtt gagct 15

<210> 87  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 87  
tctcccagcg tgcgcatat 20

<210> 88  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (8)...(8)  
<223> m5c

<221> modified\_base  
<222> (17)...(17)  
<223> m5c

- 18 -

<223> Synthetic Sequence

<400> 88  
tccatgangt tcctgangtt 20

<210> 89  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (7)...(7)  
<223> m5c

<223> Synthetic Sequence

<400> 89  
gcatgangtt gagct 15

<210> 90  
<211> 16  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 90  
tccagcgtgc gccata 16

<210> 91  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 91  
tctcccagcg tgcgcat 18

<210> 92  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 92  
tccatgagct tcctgagtct 20

<210> 93  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 93 gcatgtcgtt gagct	15
<210> 94 <211> 19 <212> DNA <213> Artificial Sequence	
<220> <223> Synthetic Sequence	
<400> 94 tcctgacgtt cctgacgtt	19
<210> 95 <211> 15 <212> DNA <213> Artificial Sequence	
<220> <223> Synthetic Sequence	
<400> 95 gcatgatgtt gagct	15
<210> 96 <211> 15 <212> DNA <213> Artificial Sequence	
<220> <223> Synthetic Sequence	
<400> 96 gcatttcgag gagct	15
<210> 97 <211> 15 <212> DNA <213> Artificial Sequence	
<220> <223> Synthetic Sequence	
<400> 97 gcatgtagct gagct	15
<210> 98 <211> 20 <212> DNA <213> Artificial Sequence	
<220> <223> Synthetic Sequence	
<400> 98 tccaggacgt tcctagttct	20
<210> 99 <211> 20 <212> DNA	

- 20 -

<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 99  
tccaggagct tcctagttct 20

<210> 100  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 100  
tccaggatgt tcctagttct 20

<210> 101  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 101  
tccagtctag gcctagttct 20

<210> 102  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 102  
tccagttcga gcctagttct 20

<210> 103  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 103  
gcatggcgtt gagct 15

<210> 104  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 104

- 21 -

gcatagcggt gagct

15

<210> 105  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

gcattgcggt gagct

15

<210> 106  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

gcttgcggtg cgttt

15

<210> 107  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

tctcccagcg ttgcgccata t

21

<210> 108  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

tctcccagcg tgcgttatat

20

<210> 109  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

tctccctgcg tgcgccatat

20

<210> 110  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 110  
tctgcgtgcg tgcgccatat 20

<210> 111  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 111  
tctcctagcg tgcgccatat 20

<210> 112  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 112  
tctcccagcg tgcgcctttt 20

<210> 113  
<211> 13  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<221> misc\_difference  
<222> (5)...(5)  
<223> n is a or g or c or t/u

<221> misc\_difference  
<222> (6)...(6)  
<223> d is a or g or t/u; not c

<221> misc\_difference  
<222> (9)...(10)  
<223> h is a or c or t/u; not g

<400> 113  
gctandcghh agc 13

<210> 114  
<211> 13  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 114



tcctgacgtt ccc

13

<210> 115  
<211> 13  
<212> DNA  
<213> Artificial Sequence

<220> .  
<223> Synthetic Sequence

ggaagacgtt aga

13

<210> 116  
<211> 13  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

tcctgacgtt aga

13

<210> 117  
<211> 27  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

tcagaccagc tggtcgggtg ttcctga

27

<210> 118  
<211> 27  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

tcaggaacac ccgaccagct ggtctga

27

<210> 119  
<211> 13  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

gctagtcgat agc

13

<210> 120  
<211> 13  
<212> DNA  
<213> Artificial Sequence

- 24 -

<220>  
<223> Synthetic Sequence

<400> 120  
gctagtcgct agc 13

<210> 121  
<211> 14  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 121  
gcttgacgctc tagc 14

<210> 122  
<211> 14  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 122  
gcttgacggtt tagc 14

<210> 123  
<211> 14  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 123  
gcttgacgctc aagc 14

<210> 124  
<211> 14  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 124  
gctagacggtt tagc 14

<210> 125  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 125  
tccatgacat tcctgatgct 20

- 25 -

<210> 126  
<211> 14  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 126  
gctagacgtc tagc 14

<210> 127  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 127  
ggctatgtcg ttcctagcc 19

<210> 128  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 128  
ggctatgtcg atcctagcc 19

<210> 129  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 129  
ctcatgggtt tctccaccaa g 21

<210> 130  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 130  
cttgggtggag aaacccatga g 21

<210> 131  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 131  
tccatgacgt tcctagttct 20

<210> 132  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 132  
ccgcttcctc cagatgagct catg 24

<210> 133  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 133  
catgagctca tctggaggaa gcgg 24

<210> 134  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 134  
ccagatgagc tcatgggttt ctcc 24

<210> 135  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 135  
ggagaaacct atgagctcat ctgg 24

<210> 136  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 136  
agcatcagga acgacatgga 20

- 27 -

<210> 137  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 137  
tccatgacgt tcctgacgtt 20  
  
<210> 138  
<211> 19  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 138  
gcgcgcgcgc gcgcgcgcgc 19  
  
<210> 139  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 139  
ccggccggcc ggccggccgg 20  
  
<210> 140  
<211> 43  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 140  
ttccaatcag cccacccgc tctggcccca ccctcaccct cca 43  
  
<210> 141  
<211> 43  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 141  
tggagggtga ggggtggggcc agâgcgggtg gggctgattg gaa 43  
  
<210> 142  
<211> 27  
<212> DNA  
<213> Artificial Sequence  
  
<220>

- 28 -

<223> Synthetic Sequence

<400> 142  
tcaaattgtgg gattttccca tgagtct 27

<210> 143  
<211> 27  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 143  
agactcatgg gaaaatccca catttga 27

<210> 144  
<211> 27  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 144  
tgccaagtgc tgagtcacta ataaaga 27

<210> 145  
<211> 27  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 145  
tctttattag tgactcagca cttggca 27

<210> 146  
<211> 31  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 146  
tgcaggaagt ccgggttttc cccaaccccc c 31

<210> 147  
<211> 31  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 147  
gggggggttg ggaaaaccg gacttcctgc a 31

<210> 148

- 29 -

<211> 38  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 148  
ggggactttc cgctggggac tttccagggg gactttcc 38

<210> 149  
<211> 45  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 149  
tccatgacgt tcctctccat gacgttcctc tccatgacgt tcctc 45

<210> 150  
<211> 45  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 150  
gaggaacgtc atggagagga acgtcatgga gaggaacgtc atgga 45

<210> 151  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 151  
ataatagagc ttcaagcaag 20

<210> 152  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 152  
tccatgacgt tcctgacgtt 20

<210> 153  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 153  
tccatgacgt tcctgacgtt 20

<210> 154  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 154  
tccaggactt tcctcaggtt 20

<210> 155  
<211> 45  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 155  
tcttgcatg ctaaaggacg tcacattgca caatcttaat aaggt 45

<210> 156  
<211> 45  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 156  
accttattaa gattgtgcaa tgtgacgtcc tttagcatcg caaga 45

<210> 157  
<211> 28  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 157  
tcctgacgtt cctggcggtc ctgtcgct 28

<210> 158  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 158  
tcctgtcgct cctgtcgct 19

<210> 159  
<211> 15



- 31 -

<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 159  
tcctgacgtt gaagt 15

<210> 160  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 160  
tcctgtcgtt gaagt 15

<210> 161  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 161  
tcctggcgtt gaagt 15

<210> 162  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 162  
tcctgccgtt gaagt 15

<210> 163  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 163  
tccttacgtt gaagt 15

<210> 164  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 164  
tcctaacggt gaagt 15

<210> 165  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 165  
tcctcacggt gaagt 15

<210> 166  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 166  
tcctgacgat gaagt 15

<210> 167  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 167  
tcctgacgct gaagt 15

<210> 168  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 168  
tcctgacggt gaagt 15

<210> 169  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 169  
tcctgacgta gaagt 15

<210> 170  
<211> 15  
<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 170  
tcctgacgtc gaagt 15

<210> 171  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 171  
tcctgacgtg gaagt 15

<210> 172  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 172  
tcctgagctt gaagt 15

<210> 173  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 173  
gggggacgtt ggggg 15

<210> 174  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 174  
tcctgacgtt ccttc 15

<210> 175  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 175

tctcccagcg agcgagcgcc at

22

<210> 176  
<211> 32  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

tcctgacgtt cccctggcgg tcccctgtcg ct

32

<210> 177  
<211> 28  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

tcctgtcgct cctgtcgctc ctgtcgct

28

<210> 178  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

tcctggcggg gaagt

15

<210> 179  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (7)...(7)  
<223> m5c

&lt;223&gt; Synthetic Sequence

tcctgangtt gaagt

15

<210> 180  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (3)...(3)  
<223> m5c

&lt;223&gt; Synthetic Sequence

<400> 180  
tcntgacggt gaagt 15

<210> 181  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 181  
tcctagcggt gaagt 15

<210> 182  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 182  
tccagacggt gaagt 15

<210> 183  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 183  
tcctgacggg gaagt 15

<210> 184  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 184  
tcctggcggg gaagt 15

<210> 185  
<211> 27  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 185  
ggctccgggg aggggaatttt tgtctat 27

<210> 186  
<211> 27

- 36 -

<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 186  
atagacaaaa attccctccc cggagcc 27

<210> 187  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 187  
tccatgagct tccttgagtc t 21

<210> 188  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 188  
tcgtcgctgt ctccgcttct t 21

<210> 189  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 189  
tcgtcgctgt ctccgcttct t 21

<210> 190  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 190  
tcgagacatt gcacaatcat ctg 23

<210> 191  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 191  
cagattgtgc aatgtctcga 20

<210> 192  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 192  
tccatgtcgt tcctgatgcg 20

<210> 193  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 193  
gcgatgtcgt tcctgatgct 20

<210> 194  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 194  
gcgatgtcgt tcctgatgcg 20

<210> 195  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 195  
tccatgtcgt tccgcgcgcg 20

<210> 196  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 196  
tccatgtcgt tcctgccgct 20

<210> 197  
<211> 20  
<212> DNA

<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 197  
tccatgtcgt tcctgtagct 20

<210> 198  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 198  
gcggcgggcg gcgcgcgccc 20

<210> 199  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 199  
atcaggaacg tcatgggaag c 21

<210> 200  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 200  
tccatgagct tcctgagtct 20

<210> 201  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 201  
tcaacggt 8

<210> 202  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 202



- 39 -

tcaagctt

8

<210> 203  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 203  
tcctgtcggt cctgtcggt

19

<210> 204  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 204  
tccatgtcgt tttgtcggt

20

<210> 205  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 205  
tcctgtcggt cctgtcggt

20

<210> 206  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 206  
tcctgtcgt tcctgtcggt

20

<210> 207  
<211> 29  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> misc\_feature  
<222> (1)...(3)  
<223> Conjugated to biotin moiety.

<223> Synthetic Sequence

<400> 207  
tccattccat gacgttcctg atgcttcca

29

- 40 -

<210> 208  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 208  
tcctgtcggtt ttttgtcggtt 20

<210> 209  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 209  
tcgtcgctgt ctccgcttct t 21

<210> 210  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 210  
tcgtcgctgt ctgcccttct t 21

<210> 211  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 211  
tcgtcgctgt tgtcgtttct t 21

<210> 212  
<211> 30  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 212  
tcctgtcggtt cctgtcggtg gaacgacagg 30

<210> 213  
<211> 40  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 213  
tcctgtcgtt cctgtcgttt caacgtcagg aacgacagga 40

<210> 214  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 214  
ggggtctgtc gttttggggg g 21

<210> 215  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 215  
ggggtctgtg cttttggggg g 21

<210> 216  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 216  
tccggccggt gaagt 15

<210> 217  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 217  
tccggacggt gaagt 15

<210> 218  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 218  
tcccgccggt gaagt 15

<210> 219

<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 219  
tccagacggt gaagt 15

<210> 220  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 220  
tcccgcggt gaagt 15

<210> 221  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 221  
tccagagctt gaagt 15

<210> 222  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (8)...(8)  
<223> m5c

<221> modified\_base  
<222> (17)...(17)  
<223> m5c

<223> Synthetic Sequence

<400> 222  
tccatgtngt tcctgtngtt 20

<210> 223  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 223  
tccatgacgt tcctgacgtt 20

<210> 224  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 224  
ggggttgacg ttttgggggg 20  
  
<210> 225  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 225  
tccaggactt ctctcaggtt 20  
  
<210> 226  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 226  
tttttttttt tttttttttt 20  
  
<210> 227  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 227  
tccatgccgt tcctgccgtt 20  
  
<210> 228  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 228  
tccatggcgg gcctggcggg 20  
  
<210> 229  
<211> 20  
<212> DNA  
<213> Artificial Sequence

- 44 -

<220>  
<223> Synthetic Sequence

<400> 229  
tccatgacgt tcctgccgtt 20

<210> 230  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 230  
tccatgacgt tcctggcggg 20

<210> 231  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 231  
tccatgacgt tcctgcgttt 20

<210> 232  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 232  
tccatgacgg tcctgacggt 20

<210> 233  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 233  
tccatgcgtg cgtgcgtttt 20

<210> 234  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 234  
tccatgcgtt gcgttgcggt 20

- 45 -

<210> 235  
<211> 30  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> misc\_feature  
<222> (1)...(3)  
<223> Conjugated to biotin moiety.

<223> Synthetic Sequence

<400> 235  
tccattccat tctaggcctg agtcttccat 30

<210> 236  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 236  
tccatagcgt tcctagcggt 20

<210> 237  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 237  
tccatgtcgt tcctgtcggt 20

<210> 238  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 238  
tccatagcga tcctagcgat 20

<210> 239  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 239  
tccattgcgt tccttgcgtt 20

<210> 240  
<211> 20

- 46 -

<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 240  
tccatagcgg tcctagcgg 20

<210> 241  
<211> 29  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 241  
tccatgattt tcctgcagtt cctgatttt 29

<210> 242  
<211> 29  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 242  
tccatgacgt tcctgcagtt cctgacgtt 29

<210> 243  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 243  
ggcggcggcg gcggcggcgg 20

<210> 244  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 244  
tccacgacgt ttctgacgtt 20

<210> 245  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence



- 47 -

<400> 245  
tcgtcgttgt cgttgtcgtt 20

<210> 246  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 246  
tcgtcgtttt gtcgttttgt cgtt 24

<210> 247  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 247  
tcgtcgttgt cgtttgtcg tt 22

<210> 248  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 248  
gcgtgcgttg tcgtgtcgt t 21

<210> 249  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<221> modified\_base  
<222> (2)...(2)  
<223> m5c

<221> modified\_base  
<222> (6)...(6)  
<223> m5c

<221> modified\_base  
<222> (10)...(10)  
<223> m5c

<221> modified\_base  
<222> (15)...(15)  
<223> m5c

<400> 249

cnggcnggcgcn gggcncgcg

19

<210> 250  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 250  
gcggcgggcg gcgcgcgccc

20

<210> 251  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<221> modified\_base  
<222> (3)...(3)  
<223> I

<221> modified\_base  
<222> (8)...(8)  
<223> I

<221> modified\_base  
<222> (14)...(14)  
<223> I

<400> 251  
agncccgnga acgnattcac

20

<210> 252  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 252  
tgtcgtttgt cgtttgtcgt t

21

<210> 253  
<211> 25  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 253  
tgtcgttgtc gttgtcgttg tcggt

25

<210> 254  
<211> 25  
<212> DNA

- 49 -

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 254

tgtcggtgtc gttgctggtg tcggt 25

<210> 255

<211> 14

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 255

tcgtcgtcgt cggt 14

<210> 256

<211> 13

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 256

tgtcggtgtc gtt 13

<210> 257

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 257

cccccccccc ccccccccc 20

<210> 258

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 258

tctagcgttt ttagcgttcc 20

<210> 259

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 259

- 50 -

tgcaccccc aggccaccat

20

<210> 260  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 260

tcgtcgtcgt cgtcgtcgtc gtt

23

<210> 261  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 261

tcgtcgttgt cgttgtcgtt

20

<210> 262  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 262

tcgtcgtttt gtcgttttgt cgtt

24

<210> 263  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 263

tcgtcgttgt cgttttgtcg tt

22

<210> 264  
<211> 39  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 264

ggggagggag gaacttctta aaattccccc agaattgttt

39

<210> 265  
<211> 39  
<212> DNA  
<213> Artificial Sequence

- 51 -

<220>  
<223> Synthetic Sequence

<400> 265  
aaacattctg ggggaatttt aagaagttcc tccctcccc 39

<210> 266  
<211> 33  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 266  
atgtttactt cttaaaattc ccccagaatg ttt 33

<210> 267  
<211> 33  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 267  
aaacattctg ggggaatttt aagaagtaaa cat 33

<210> 268  
<211> 33  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 268  
atgtttacta gacaaaattc ccccagaatg ttt 33

<210> 269  
<211> 33  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 269  
aaacattctg ggggaatttt gtctagtaaa cat 33

<210> 270  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 270  
aaaattgacg ttttaaaaaa 20

- 52 -

<210> 271  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 271  
ccccttgacg ttttcccccc 20  
  
<210> 272  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 272  
ttttcgttgt ttttgtcggt 20  
  
<210> 273  
<211> 24  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 273  
tcgtcgtttt gtcgttttgc cggt 24  
  
<210> 274  
<211> 14  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 274  
ctgcagcctg ggac 14  
  
<210> 275  
<211> 25  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 275  
accgcgtcgta attatagtaa aaccc 25  
  
<210> 276  
<211> 21  
<212> DNA  
<213> Artificial Sequence

- 53 -

<220>  
<223> Synthetic Sequence

<400> 276  
ggtacctgtg gggacattgt g 21

<210> 277  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 277  
agcacccaac gtgagagg 18

<210> 278  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 278  
tccatgccgt tcctgccgtt 20

<210> 279  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 279  
tccatgacgg tcctgacggt 20

<210> 280  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 280  
tccatgccgg tcctgccggt 20

<210> 281  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 281  
tccatgcgcg tcctgcgct 20

- 54 -

<210> 282  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 282  
ctggtctttc tgggtttttt ctgg 24

<210> 283  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 283  
tcaggggtgg ggggaacctt 20

<210> 284  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (8)...(8)  
<223> m5c

<223> Synthetic Sequence

<400> 284  
tccatgangt tcctagttct 20

<210> 285  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 285  
tccatgatgt tcctagttct 20

<210> 286  
<211> 26  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 286  
cccgaagtca tttcctctta acctgg 26

<210> 287  
<211> 26



- 55 -

<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 287  
ccagggttaag aggaaatgac ttcggg 26

<210> 288  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (7)...(7)  
<223> m5c

<223> Synthetic Sequence

<400> 288  
tcctggngggg gaagt 15

<210> 289  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (2)...(2)  
<223> m5c

<221> modified\_base  
<222> (5)...(5)  
<223> m5c

<221> modified\_base  
<222> (9)...(9)  
<223> m5c

<221> modified\_base  
<222> (12)...(12)  
<223> m5c

<221> modified\_base  
<222> (14)...(14)  
<223> m5c

<221> modified\_base  
<222> (16)...(16)  
<223> m5c

<223> Synthetic Sequence

<400> 289  
gnggngggng gngngngccc 20

<210> 290  
<211> 20

- 56 -

<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 290  
tccatgtgct tcctgatgct 20  
  
<210> 291  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 291  
tccatgtcct tcctgatgct 20  
  
<210> 292  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 292  
tccatgtcgt tcctagttct 20  
  
<210> 293  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 293  
tccaagtagt tcctagttct 20  
  
<210> 294  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 294  
tccatgtagt tcctagttct 20  
  
<210> 295  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence

- 57 -

<400> 295  
tcccgcgcgt tccgcgcgtt 20

<210> 296  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 296  
tcctggcgcgt cctggcgcgtt 20

<210> 297  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 297  
tcctggaggg gaagt 15

<210> 298  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 298  
tcctgggggg gaagt 15

<210> 299  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 299  
tcctggtggg gaagt 15

<210> 300  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 300  
tcgtcgtttt gtcgttttgt cggt 24

<210> 301  
<211> 24  
<212> DNA

- 58 -

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 301  
ctggtctttc tggttttttt ctgg 24

<210> 302  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 302  
tccatgacgt tcctgacgtt 20

<210> 303  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 303  
tccaggactt ctctcaggtt 20

<210> 304  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<221> modified\_base  
<222> (2)...(2)  
<223> m5c

<221> modified\_base  
<222> (5)...(5)  
<223> m5c

<221> modified\_base  
<222> (13)...(13)  
<223> m5c

<221> modified\_base  
<222> (21)...(21)  
<223> m5c

<400> 304  
tngtngtttt gtngttttgt ngtt 24

<210> 305  
<211> 29  
<212> DNA  
<213> Artificial Sequence

- 59 -

<220>  
<221> misc\_feature  
<222> (1)...(3)  
<223> Conjugated to biotin moiety.

<223> Synthetic Sequence

<400> 305  
tcgtcgtttt gtcgttttgt cgttttttt 29

<210> 306  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 306  
gctatgacgt tccaaggg 18

<210> 307  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 307  
tcaacggt 8

<210> 308  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 308  
tccaggactt tcctcaggtt 20

<210> 309  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 309  
ctctctgtag gcccgcttgg 20

<210> 310  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>

- 60 -

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 310

ctttccgttg gaccctggg

20

&lt;210&gt; 311

&lt;211&gt; 20

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 311

gtccgggcca ggccaaagtc

20

&lt;210&gt; 312

&lt;211&gt; 20

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 312

gtgcgcgcga gcccgaaatc

20

&lt;210&gt; 313

&lt;211&gt; 20

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;221&gt; modified\_base

&lt;222&gt; (8)...(8)

&lt;223&gt; I

&lt;221&gt; modified\_base

&lt;222&gt; (17)...(17)

&lt;223&gt; I

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 313

tccatgangt tcctgangtt

20

&lt;210&gt; 314

&lt;211&gt; 20

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 314

aatagtcgcc ataacaaaac

20

&lt;210&gt; 315

&lt;211&gt; 20

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 315  
aatagtcgcc atggcggggc 20

<210> 316  
<211> 28  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> misc\_difference  
<222> (1)...(3)  
<223> Biotin moiety attached at 5' end of sequence.

<223> Synthetic Sequence

<400> 316  
tttttccatg tcgttcctga tgcttttt 28

<210> 317  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 317  
tcctgtcgtt gaagtttttt 20

<210> 318  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 318  
gctagcttta gagctttaga gctt 24

<210> 319  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 319  
tgctgcttcc cccccccccc 20

<210> 320  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>

- 62 -

<223> Synthetic Sequence

<400> 320  
tcgacgttcc ccccccccc 20

<210> 321  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 321  
tcgtcgttcc ccccccccc 20

<210> 322  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 322  
tcgtcgttcc ccccccccc 20

<210> 323  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 323  
tcgccgttcc ccccccccc 20

<210> 324  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 324  
tcgtcgatcc ccccccccc 20

<210> 325  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 325  
tcctgacgtt gaagt 15

<210> 326



- 63 -

<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 326  
tcctgccggt gaagt 15

<210> 327  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 327  
tcctgacggt gaagt 15

<210> 328  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 328  
tcctgagctt gaagt 15

<210> 329  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 329  
tcctggcggg gaagt 15

<210> 330  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 330  
aaaatctgtg cttttaaaaa a 21

<210> 331  
<211> 33  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

- 64 -

<400> 331  
gatccagtca cagtgacctg gcagaatctg gat 33

<210> 332  
<211> 33  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 332  
gatccagatt ctgccaggtc actgtgactg gat 33

<210> 333  
<211> 33  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 333  
gatccagtca cagtgactca gcagaatctg gat 33

<210> 334  
<211> 33  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 334  
gatccagatt ctgctgagtc actgtgactg gat 33

<210> 335  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (16)...(16)  
<223> m5c

<223> Synthetic Sequence

<400> 335  
tcgtcgttcc ccccncccc 20

<210> 336  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (2)...(2)  
<223> m5c

- 65 -

<221> modified\_base  
<222> (5)...(5)  
<223> m5c  
  
<223> Synthetic Sequence  
  
<400> 336  
tngtngttcc cccccccccc 20  
  
<210> 337  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<221> modified\_base  
<222> (2)...(2)  
<223> m5c  
  
<223> Synthetic Sequence  
  
<400> 337  
tngtcgttcc cccccccccc 20  
  
<210> 338  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<221> modified\_base  
<222> (5)...(5)  
<223> m5c  
  
<223> Synthetic Sequence  
  
<400> 338  
tcgtngttcc cccccccccc 20  
  
<210> 339  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 339  
tcgtcggtcc cccccccccc 20  
  
<210> 340  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 340  
tcgtcggtcc cccccccccc 20

<210> 341  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 341  
tcggcggttcc cccccccccc 20  
  
<210> 342  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 342  
ggccttttcc cccccccccc 20  
  
<210> 343  
<211> 24  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 343  
tcgtcgtttt gacgttttgt cgtt 24  
  
<210> 344  
<211> 24  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 344  
tcgtcgtttt gacgttttga cgtt 24  
  
<210> 345  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 345  
ccgtcggttcc cccccccccc 20  
  
<210> 346  
<211> 20  
<212> DNA  
<213> Artificial Sequence

- 67 -

<220>  
<223> Synthetic Sequence

<400> 346  
gcgtcgttcc cccccccccc 20

<210> 347  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 347  
tcgtcattcc cccccccccc 20

<210> 348  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 348  
acgtcgttcc cccccccccc 20

<210> 349  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 349  
ctgtcgttcc cccccccccc 20

<210> 350  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> misc\_feature  
<222> (1)...(3)  
<223> Biotin moiety attached at 5' end of sequence.

<223> Synthetic Sequence

<400> 350  
tttttcgtcg ttcccccccc cccc 24

<210> 351  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> misc\_feature

<222> (18)...(20)  
<223> Biotin moiety attached at 3' end of sequence.

<223> Synthetic Sequence

<400> 351  
tcgtcgttcc cccccccccc 20

<210> 352  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> misc\_feature  
<222> (22)...(24)  
<223> Biotin moiety attached at 3' end of sequence.

<223> Synthetic Sequence

<400> 352  
tcgtcgtttt gtcgttttgt cggt 24

<210> 353  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 353  
tcagttcct tcctcagttc 20

<210> 354  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (2)...(2)  
<223> m5c

<223> Synthetic Sequence

<400> 354  
tngtcgtttt gtcgttttgt cggt 24

<210> 355  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 355  
tcctggaggg gaagt 15

<210> 356

<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 356  
tcctgaaaag gaagt 15

<210> 357  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 357  
tcgtcgttcc cccccc 17

<210> 358  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<221> modified\_base  
<222> (2)...(2)  
<223> m5c

<221> modified\_base  
<222> (5)...(5)  
<223> m5c

<221> modified\_base  
<222> (13)...(13)  
<223> m5c

<221> modified\_base  
<222> (21)...(21)  
<223> m5c

<400> 358  
tngtngtttt gtngttttgt ngtt 24

<210> 359  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 359  
ggggtcaagc ttgagggggg 20

<210> 360  
<211> 20

- 70 -

<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 360  
tgctgcttcc ccccccccc 20

<210> 361  
<211> 14  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 361  
tcgtcgtcgt cggt 14

<210> 362  
<211> 14  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 362  
tcgtcgtcgt cggt 14

<210> 363  
<211> 14  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 363  
tcgtcgtcgt cggt 14

<210> 364  
<211> 10  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 364  
tcaacgttga 10

<210> 365  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence



- 71 -

<400> 365  
tcaacggt 8

<210> 366  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 366  
atagttttcc atttttttac 20

<210> 367  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 367  
aatagtcgcc atcgcgcgac 20

<210> 368  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 368  
aatagtcgcc atcccgggac 20

<210> 369  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 369  
aatagtcgcc atccccccc 20

<210> 370  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 370  
tgctgctttt gtgcttttgt gctt 24

<210> 371  
<211> 24  
<212> DNA

- 72 -

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 371

ctgtgctttc tgtgtttttc tgtg 24

<210> 372

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 372

ctaactctttc taattttttt ctaa 24

<210> 373

<211> 26

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 373

tcgtcgttgg tgtcgttggt gtcggt 26

<210> 374

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 374

tcgtcgttgg ttgtcgtttt gggt 24

<210> 375

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 375

accatggacg agctgtttcc cctc 24

<210> 376

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 376

- 73 -

tcgtcggtttt gcgtgcgttt

20

<210> 377  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 377

ctgtaagtga gcttggagag

20

<210> 378  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 378

gagaacgctg gaccttcc

18

<210> 379  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 379

cgggcgactc agtctatcgg

20

<210> 380  
<211> 37  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 380

gttctcagat aaagcggaac cagcaacaga cacagaa

37

<210> 381  
<211> 37  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 381

ttctgtgtct gttgctggtt ccgctttatc tgagaac

37

<210> 382  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 382  
cagacacaga agcccgatag acg 23

<210> 383  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 383  
agacagacac gaaacgaccg 20

<210> 384  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 384  
gtctgtccca tgatctcgaa 20

<210> 385  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 385  
gctggccagc ttacctcccg 20

<210> 386  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 386  
ggggcctcta tacaacctgg g 21

<210> 387  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 387  
ggggtccctg agactgcc 18

- 75 -

<210> 388  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 388  
gagaacgctg gaccttccat 20  
  
<210> 389  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 389  
tccatgtcgg tcctgatgct 20  
  
<210> 390  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 390  
ctcttgcgac ctggaaggta 20  
  
<210> 391  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 391  
aggtagagcc aggactacga 20  
  
<210> 392  
<211> 24  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 392  
accatggacg acctgtttcc cctc 24  
  
<210> 393  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 393  
accatggatt acctttttcc cctt 24

<210> 394  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 394  
atggaaggtc cagcgttctc 20

<210> 395  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 395  
agcatcagga cgcacatgga 20

<210> 396  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence .

<400> 396  
ctctccaagc tcacttacag 20

<210> 397  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 397  
tccctgagac tgccccacct t 21

<210> 398  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 398  
gccaccaaaa cttgtccatg 20

- 77 -

<210> 399  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 399  
gtccatggcg tgcgggatga 20  
  
<210> 400  
<211> 19  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 400  
cctctataca acctgggac 19  
  
<210> 401  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 401  
cgggcgactc agtctatcgg 20  
  
<210> 402  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 402  
gcgctaccgg tagcctgagt 20  
  
<210> 403  
<211> 35  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 403  
cgactgccga acaggatatc ggtgatcagc actgg 35  
  
<210> 404  
<211> 35  
<212> DNA  
<213> Artificial Sequence  
  
<220>

- 78 -

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 404

ccagtgctga tcaccgatat cctgttcggc agtcg

35

&lt;210&gt; 405

&lt;211&gt; 17

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 405

ccaggttgta tagaggc

17

&lt;210&gt; 406

&lt;211&gt; 18

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 406

tctcccagcg tacgccat

18

&lt;210&gt; 407

&lt;211&gt; 18

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 407

tctcccagcg tgcgtttt

18

&lt;210&gt; 408

&lt;211&gt; 18

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 408

tctcccagcg tgcgccat

18

&lt;210&gt; 409

&lt;211&gt; 18

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 409

tctcccgtcg tgcgccat

18

&lt;210&gt; 410



- 79 -

<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 410  
ataatcgtcg ttcaagcaag 20  
  
<210> 411  
<211> 23  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 411  
tcgtcgtttt gtcgttttgt cgt 23  
  
<210> 412  
<211> 24  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 412  
tcgtcgtttt gtcgttttgt cggt 24  
  
<210> 413  
<211> 24  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 413  
tcgtcgtttt gtcgttttgt cggt 24  
  
<210> 414  
<211> 24  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<221> misc\_difference  
<222> (3)...(3)  
<223> n is a or c or g or t/u  
  
<221> misc\_difference  
<222> (8)...(8)  
<223> n is a or c or g or t/u  
  
<221> misc\_difference  
<222> (11)...(11)  
<223> n is a or c or g or t/u

- 80 -

<221> misc\_difference  
<222> (16)...(16)  
<223> n is a or c or g or t/u

<221> misc\_difference  
<222> (19)...(19)  
<223> n is a or c or g or t/u

<221> misc\_difference  
<222> (24)...(24)  
<223> n is a or c or g or t/u

<223> Synthetic Sequence

<400> 414  
tcntcgnttt ntcgtnttnt cgtn 24

<210> 415  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 415  
tctcccagcg tcgccat 17

<210> 416  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 416  
tctcccacg tcgccat 17

<210> 417  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 417  
ataatcgtgc gttcaagaaa g 21

<210> 418  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 418  
ataatcgacg ttcccccccc 20

- 81 -

<210> 419  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 419  
tctatcgacg ttcaagcaag 20  
  
<210> 420  
<211> 14  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 420  
tcctgacggg gagt 14  
  
<210> 421  
<211> 19  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 421  
tccatgacgt tcctgatcc 19  
  
<210> 422  
<211> 19  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 422  
tccatgacgt tcctgatcc 19  
  
<210> 423  
<211> 19  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 423  
tccatgacgt tcctgatcc 19  
  
<210> 424  
<211> 15  
<212> DNA  
<213> Artificial Sequence  
  
<220>

<223> Synthetic Sequence

<400> 424  
tcctggcgtg gaagt 15

<210> 425  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 425  
tccatgacgt tcctgatcc 19

<210> 426  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 426  
tcgtcgtgt tgcgtttct t 21

<210> 427  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 427  
agcagcttta gagctttaga gctt 24

<210> 428  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 428  
cccccccccc ccccccccc cccc 24

<210> 429  
<211> 32  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 429  
tcgtcgtttt gtcgttttgt cgttttgcg tt 32

<210> 430

- 83 -

<211> 28  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 430  
tcgtcgtttt ttgtcgtttt ttgtcgtt 28

<210> 431  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 431  
tcgtcgtttt tttttttttt 20

<210> 432  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 432  
tttttcaacg ttgatttttt 20

<210> 433  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 433  
tttttttttt tttttttttt tttt 24

<210> 434  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 434  
ggggtcgtcg ttttgggggg 20

<210> 435  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

- 84 -

<400> 435  
tcgtcgtttt gtcgttttgg gggg 24  
<210> 436  
<211> 27  
<212> DNA  
<213> Artificial Sequence  
<220>  
<223> Synthetic Sequence  
<400> 436  
tcgtcgctgt ctccgcttct tcttgcc 27  
<210> 437  
<211> 15  
<212> DNA  
<213> Artificial Sequence  
<220>  
<223> Synthetic Sequence  
<400> 437  
tcgtcgctgt ctccg 15  
<210> 438  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
<220>  
<223> Synthetic Sequence  
<400> 438  
ctgtaagtga gcttgagag 20  
<210> 439  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
<220>  
<223> Synthetic Sequence  
<400> 439  
gagaacgctg gaccttccat 20  
<210> 440  
<211> 17  
<212> DNA  
<213> Artificial Sequence  
<220>  
<223> Synthetic Sequence  
<400> 440  
ccaggttgta tagaggc 17  
<210> 441  
<211> 17

- 85 -

<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 441  
gctagacgtt agcgtga 17

<210> 442  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 442  
ggagctcttc gaacgccata 20

<210> 443  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 443  
tctccatgat ggttttatcg 20

<210> 444  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 444  
aaggtggggc agtctcaggg a 21

<210> 445  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 445  
atcggaggac tggcgcgccg 20

<210> 446  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

- 86 -

<400> 446  
ttaggacaag gtctaggggtg 20  
  
<210> 447  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 447  
accacaacga gaggaacgca 20  
  
<210> 448  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 448  
ggcagtgacg gctcaccggg 20  
  
<210> 449  
<211> 17  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 449  
gaaccttcca tgctgtt 17  
  
<210> 450  
<211> 17  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 450  
gctagacgtt agcgtga 17  
  
<210> 451  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 451  
gcttgagggg cctgtaagtg 20  
  
<210> 452  
<211> 12  
<212> DNA



- 87 -

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 452  
gtagccttcc ta 12

<210> 453  
<211> 14  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 453  
cggtagcctt ccta 14

<210> 454  
<211> 16  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 454  
cacggtagcc ttccta 16

<210> 455  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 455  
agcacggtag ccttccta 18

<210> 456  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 456  
gaacgctgga ccttccat 18

<210> 457  
<211> 10  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 457

gaccttccat

10

<210> 458  
<211> 12  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 458

tggaccttcc at

12

<210> 459  
<211> 14  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 459

gctggacctt ccat

14

<210> 460  
<211> 16  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 460

acgctggacc ttccat

16

<210> 461  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 461

taagctctgt caagccagg

20

<210> 462  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 462

gagaacgctg gaccttccat gt

22

<210> 463  
<211> 20  
<212> DNA  
<213> Artificial Sequence

- 89 -

<220>  
<223> Synthetic Sequence

<400> 463  
tccatgtcgg tcctgatgct 20

<210> 464  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 464  
ttcatgcctt gcaaaatggc g 21

<210> 465  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 465  
tgctagctgt gcctgtacct 20

<210> 466  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 466  
agcatcagga ccgacatgga 20

<210> 467  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 467  
gaccttccat gtcggtcctg at 22

<210> 468  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 468  
acaaccacga gaacgggaac 20

- 90 -

<210> 469  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 469  
gaaccttcca tgctgttccg 20

<210> 470  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 470  
caatcaatct gaggagaccc 20

<210> 471  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 471  
tcagctctgg tactttttca 20

<210> 472  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 472  
tggttacggt ctgtcccatg 20

<210> 473  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 473  
gtctatcgga ggactggcgc 20

<210> 474  
<211> 20  
<212> DNA  
<213> Artificial Sequence

- 91 -

<220>  
<223> Synthetic Sequence

<400> 474  
cattttacgg gcgggcgggc 20

<210> 475  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 475  
gaggggacca ttttacgggc 20

<210> 476  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 476  
tgtccagccg aggggaccat 20

<210> 477  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 477  
cgggcttacg gcggatgctg 20

<210> 478  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 478  
tggaccttct atgtcgggcc 20

<210> 479  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 479  
tgtcccatgt ttttagaagc 20

- 92 -

<210> 480  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 480  
gtggttacgg tcgtgcccacat 20  
  
<210> 481  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 481  
cctccaaatg aaagaccccc 20  
  
<210> 482  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 482  
ttgtactctc catgatggtt 20  
  
<210> 483  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 483  
ttccatgctg ttccggctgg 20  
  
<210> 484  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 484  
gaccttctat gtcggtcctg 20  
  
<210> 485  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>

<223> Synthetic Sequence

<400> 485  
gagaccgctc gaccttcgat 20

<210> 486  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 486  
ttgccccata ttttagaaac 20

<210> 487  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 487  
ttgaaactga ggtgggac 18

<210> 488  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 488  
ctatcggagg actggcgcg c 21

<210> 489  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 489  
cttgaggggc ctcccggcgg 20

<210> 490  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 490  
gctgaacctt ccatgctgtt 20

<210> 491

- 94 -

<211> 32  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 491  
tagaaacagc attcttcttt tagggcagca ca 32

<210> 492  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 492  
agatggttct cagataaagc ggaa 24

<210> 493  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 493  
ttccgcttta tctgagaacc atct 24

<210> 494  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 494  
gtcccagggtt gtatagaggc tgc 23

<210> 495  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 495  
gcgccagtcc tccgatagac 20

<210> 496  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence



- 95 -

<400> 496  
atcggaggac tggcgcgccg 20

<210> 497  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 497  
ggtctgtccc atatttttag 20

<210> 498  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 498  
tttttcaacg ttgagggggg 20

<210> 499  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 499  
tttttcaagc gttgattttt t 21

<210> 500  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 500  
ggggtcaacg ttgatttttt 20

<210> 501  
<211> 25  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 501  
ggggttttca acgttttgag ggggg 25

<210> 502  
<211> 20

- 96 -

<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 502  
ggttacggtc tgtcccatat 20

<210> 503  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 503  
ctgtcccata tttttagaca 20

<210> 504  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 504  
accatcctga ggccattcgg 20

<210> 505  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 505  
cgtctatcgg gcttctgtgt ctg 23

<210> 506  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 506  
ggccatccca cattgaaagt t 21

<210> 507  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

- 97 -

<400> 507  
ccaaatatcg gtggtcaagc ac 22

<210> 508  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 508  
gtgcttgacc accgatattt gg 22

<210> 509  
<211> 26  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 509  
gtgctgatca ccgatatcct gttcgg 26

<210> 510  
<211> 27  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 510  
ggccaacttt caatgtggga tggcctc 27

<210> 511  
<211> 27  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 511  
ttccgcgaa tggcctcagg atgggtac 27

<210> 512  
<211> 36  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 512  
tatagtcctt gagactgccc caccttctca acaacc 36

<210> 513  
<211> 27  
<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 513  
gcagcctcta tacaacctgg gacggga 27

<210> 514  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 514  
ctatcgagg actggcgcg c 22

<210> 515  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 515  
tatcgaggga ctggcgcgcc g 21

<210> 516  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 516  
gatcgaggga ctggcgcgcc g 21

<210> 517  
<211> 26  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 517  
ccgaacagga tatcggtgat cagcac 26

<210> 518  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 518

- 99 -

ttttggggtc aacgttgagg gggg

24

<210> 519  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 519

ggggtcaacg ttgagggggg

20

<210> 520  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 520

cgcgcgcgcg cgcgcgcgcg

20

<210> 521  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 521

ggggcatgac gttcgggggg

20

<210> 522  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 522

ggggcatgac gttcaaaaaa

20

<210> 523  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 523

ggggcatgag cttegggggg

20

<210> 524  
<211> 20  
<212> DNA  
<213> Artificial Sequence

- 100 -

<220>  
<223> Synthetic Sequence

<400> 524  
ggggcatgac gttcgggggg 20

<210> 525  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 525  
aaaacatgac gttcaaaaaa 20

<210> 526  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 526  
aaaacatgac gttcgggggg 20

<210> 527  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 527  
ggggcatgac gttcaaaaaa 20

<210> 528  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 528  
accatggacg atctgtttcc cctc 24

<210> 529  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 529  
gccatggacg aactgttccc cctc 24

<210> 530  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 530  
cccccccccc ccccccccccc 20

<210> 531  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 531  
gggggggggg ggggggggggg 20

<210> 532  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 532  
gctgtaaaat gaatcgcccg 20

<210> 533  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 533  
ttcgggcgga ctctccatt 20

<210> 534  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 534  
tatgccgcgc ccggacttat 20

<210> 535  
<211> 20  
<212> DNA  
<213> Artificial Sequence

- 102 -

<220>  
<223> Synthetic Sequence

<400> 535  
ggggtaatcg atcagggggg 20

<210> 536  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 536  
tttgagaacg ctggaccttc 20

<210> 537  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 537  
gatcgtgat ctaatgctcg 20

<210> 538  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 538  
gtcgtcctg atgctgttcc 20

<210> 539  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 539  
tcgtcgtcag ttcgctgtcg 20

<210> 540  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 540  
ctggaccttc catgtcgg 18



- 103 -

<210> 541  
<211> 17  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 541  
gctcggttcag cgcgtct 17  
  
<210> 542  
<211> 16  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 542  
ctggaccttc catgtc 16  
  
<210> 543  
<211> 16  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 543  
cactgtcctt cgtcga 16  
  
<210> 544  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 544  
cgctggacct tccatgtcgg 20  
  
<210> 545  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 545  
gctgagctca tgccgtctgc 20  
  
<210> 546  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>

- 104 -

<223> Synthetic Sequence

<400> 546  
aacgctggac cttccatgtc 20

<210> 547  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 547  
tgcatgccgt acacagctct 20

<210> 548  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 548  
ccttccatgt cggtcctgat 20

<210> 549  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 549  
tactcttcgg atcccttgcg 20

<210> 550  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 550  
ttccatgtcg gtcctgat 18

<210> 551  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 551  
ctgattgctc tctcgtga 18

<210> 552

- 105 -

<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 552  
ggcgttattc ctgactcgcc 20  
  
<210> 553  
<211> 22  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 553  
cctacgttgt atgcgccag ct 22  
  
<210> 554  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 554  
ggggtaatcg atgagggggg 20  
  
<210> 555  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 555  
ttcgggcgga ctctccatt 20  
  
<210> 556  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 556  
tttttttttt tttttttttt 20  
  
<210> 557  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence

- 106 -

<400> 557  
gggggttttt ttttggggg 20

<210> 558  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 558  
tttttggggg gggggttttt 20

<210> 559  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 559  
gggggggggg ggggggggt 19

<210> 560  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 560  
aaaaaaaaa aaaaaaaaaa 20

<210> 561  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 561  
cccccaaaaa aaaaaccccc 20

<210> 562  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 562  
aaaaaccccc cccccaaaaa 20

<210> 563  
<211> 27

- 107 -

<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 563  
tttgaattca ggactggtga ggttgag 27  
  
<210> 564  
<211> 27  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 564  
tttgaatcct cagcgggtctc cagtggc 27  
  
<210> 565  
<211> 45  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 565  
aattctctat cggggcttct gtgtctgttg ctggttccgc tttat 45  
  
<210> 566  
<211> 45  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 566  
ctagataaag cggaaccagc aacagacaca gaagccccga tagag 45  
  
<210> 567  
<211> 28  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 567  
ttttctagag aggtgcacaa tgctctgg 28  
  
<210> 568  
<211> 29  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence

- 108 -

<400> 568  
tttgaattcc gtgtacagaa gcgagaagc 29

<210> 569  
<211> 31  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 569  
tttgcgccg ctagacttaa cctgagagat a 31

<210> 570  
<211> 29  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 570  
tttgggcca cgagagacag agacacttc 29

<210> 571  
<211> 29  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 571  
tttgggcccg cttctcgctt ctgtacacg 29

<210> 572  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 572  
gagaacgctg gaccttccat 20

<210> 573  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 573  
tccatgtcgg tcctgatgct 20

<210> 574  
<211> 6  
<212> DNA

- 109 -

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 574

ctgtcg 6

<210> 575

<211> 6

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 575

tcgtga 6

<210> 576

<211> 6

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 576

cgtcga 6

<210> 577

<211> 6

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 577

agtgct 6

<210> 578

<211> 6

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 578

ctgtcg 6

<210> 579

<211> 6

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 579

- 110 -

agtgct

6

<210> 580  
<211> 6  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 580

cgtcga

6

<210> 581  
<211> 6  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 581

tcgtga

6

<210> 582  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 582

gagaacgctc cagcttcgat

20

<210> 583  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 583

gctagacgta agcgtga

17

<210> 584  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 584

gagaacgctc gaccttccat

20

<210> 585  
<211> 21  
<212> DNA  
<213> Artificial Sequence



- 111 -

<220>  
<223> Synthetic Sequence

<400> 585  
gagaacgctg gacctatcca t 21

<210> 586  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 586  
gctagaggtt agcgtga 17

<210> 587  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 587  
gagaacgctg gacttccat 19

<210> 588  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 588  
tcacgctaac gtctagc 17

<210> 589  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> misc\_feature  
<222> (1)...(3)  
<223> Conjugated to biotin moiety.

<223> Synthetic Sequence

<400> 589  
gctagacgtt agcgtga 17

<210> 590  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>

- 112 -

<223> Synthetic Sequence

<400> 590  
atggaaggctc gacggttctc 20

<210> 591  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 591  
gagaacgctg gaccttcgat 20

<210> 592  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 592  
gagaacgatg gaccttccat 20

<210> 593  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 593  
gagaacgctg gatccat 17

<210> 594  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 594  
gagaacgctc cagcactgat 20

<210> 595  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 595  
tccatgtcgg tcctgctgat 20

<210> 596

- 113 -

<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 596  
atgtcctcgg tcctgatgct 20  
  
<210> 597  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 597  
gagaacgctc caccttccat 20  
  
<210> 598  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 598  
gagaacgctg gaccttcgta 20  
  
<210> 599  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<221> misc\_feature  
<222> (1)...(3)  
<223> Conjugated to biotin moiety.  
  
<223> Synthetic Sequence  
  
<400> 599  
atggaaggctc cagcggttctc 20  
  
<210> 600  
<211> 6  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 600  
tcctga 6  
  
<210> 601  
<211> 8  
<212> DNA

- 114 -

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 601

tcaacgtt 8

<210> 602

<211> 6

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 602

aacgtt 6

<210> 603

<211> 8

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 603

aacgttga 8

<210> 604

<211> 17

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 604

tcacgctaac ctctagc 17

<210> 605

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 605

gagaacgctg gaccttgcac 20

<210> 606

<211> 14

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 606

- 115 -

gctggacctt ccat 14

<210> 607  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 607  
gagaacgctg gacctcatcc at 22

<210> 608  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 608  
gagaacgctg gacgctcatc cat 23

<210> 609  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 609  
aacgttgagg ggcac 15

<210> 610  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 610  
atgccccctca acgtt 15

<210> 611  
<211> 10  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 611  
tcaacgttga 10

<210> 612  
<211> 14  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 612  
gctggacctt ccat 14

<210> 613  
<211> 7  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 613  
caacggtt 7

<210> 614  
<211> 10  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 614  
acaacggtga 10

<210> 615  
<211> 6  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 615  
tcacgt 6

<210> 616  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 616  
tcaagctt 8

<210> 617  
<211> 6  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 617  
tcgtca 6

- 117 -

<210> 618  
<211> 8  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 618  
aggatatc 8  
  
<210> 619  
<211> 8  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 619  
tagacgtc 8  
  
<210> 620  
<211> 8  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 620  
gacgtcat 8  
  
<210> 621  
<211> 8  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 621  
ccatcgat 8  
  
<210> 622  
<211> 8  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 622  
atcgatgt 8  
  
<210> 623  
<211> 8  
<212> DNA  
<213> Artificial Sequence

- 118 -

<220>  
<223> Synthetic Sequence

<400> 623  
atgcatgt 8

<210> 624  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 624  
ccatgcat 8

<210> 625  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 625  
agcgctga 8

<210> 626  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 626  
tcagcgct 8

<210> 627  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 627  
ccttcgat 8

<210> 628  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 628  
gtgcgggggt ctccgggc 18



- 119 -

<210> 629  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 629  
gctgtggggc ggctcctg

18

<210> 630  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> misc\_feature  
<222> (1)...(3)  
<223> Conjugated to biotin moiety.

<223> Synthetic Sequence

<400> 630  
tcaacggtt

8

<210> 631  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> misc\_feature  
<222> (1)...(3)  
<223> Conjugated to FITC moiety.

<223> Synthetic Sequence

<400> 631  
tcaacggtt

8

<210> 632  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> misc\_feature  
<222> (1)...(3)  
<223> Conjugated to FITC moiety.

<223> Synthetic Sequence

<400> 632  
aacgttga

8

<210> 633  
<211> 7  
<212> DNA  
<213> Artificial Sequence

- 120 -

<220>  
<223> Synthetic Sequence

<400> 633  
tcaacgt 7

<210> 634  
<211> 7  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 634  
aacgttg 7

<210> 635  
<211> 6  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 635  
cgacga 6

<210> 636  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 636  
tcaacgtt 8

<210> 637  
<211> 5  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 637  
tcgga 5

<210> 638  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 638  
agaacgtt 8

- 121 -

<210> 639  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 639  
tcatcgat 8

<210> 640  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 640  
taaacggt 8

<210> 641  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 641  
ccaacggt 8

<210> 642  
<211> 6  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 642  
gctcga 6

<210> 643  
<211> 6  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 643  
cgacgt 6

<210> 644  
<211> 6  
<212> DNA  
<213> Artificial Sequence

<220>

- 122 -

<223> Synthetic Sequence

<400> 644  
cgtcgt 6

<210> 645  
<211> 6  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 645  
acgtgt 6

<210> 646  
<211> 6  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 646  
cgttcg 6

<210> 647  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 647  
gagcaagctg gaccttccat - 20

<210> 648  
<211> 6  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 648  
cgcgta 6

<210> 649  
<211> 6  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 649  
cgtacg 6

<210> 650

- 123 -

<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 650  
tcaccggt 8

<210> 651  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 651  
caagagatgc taacaatgca 20

<210> 652  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 652  
acccatcaat agctctgtgc 20

<210> 653  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 653  
ccatcgat 8

<210> 654  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 654  
tcgacgtc 8

<210> 655  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 655  
ctagcgct 8

<210> 656  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 656  
taagcgct 8

<210> 657  
<211> 13  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 657  
tcgcgaattc gcg 13

<210> 658  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 658  
atggaaggctc cagcgttct 19

<210> 659  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 659  
actggacggtt agcgtga 17

<210> 660  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 660  
cgcctggggc tggctctgg 18

<210> 661  
<211> 18

- 125 -

<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 661  
gtgtcgggggt ctccgggc 18

<210> 662  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 662  
gtgccgggggt ctccgggc 18

<210> 663  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 663  
cgccgtcgcg gcggttgg 18

<210> 664  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 664  
gaagttcacg ttgaggggca t 21

<210> 665  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 665  
atctggtgag ggcaagctat g 21

<210> 666  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

- 126 -

<400> 666  
gttgaaaccc gagaacatca t 21

<210> 667  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 667  
gcaacggt 8

<210> 668  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 668  
gtaacggt 8

<210> 669  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 669  
cgaacggt 8

<210> 670  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 670  
gaaacggt 8

<210> 671  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 671  
caaacggt 8

<210> 672  
<211> 8  
<212> DNA



- 127 -

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 672

ctaacgtt 8

<210> 673

<211> 8

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 673

ggaacgtt 8

<210> 674

<211> 8

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 674

tgaacgtt 8

<210> 675

<211> 8

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 675

acaacgtt 8

<210> 676

<211> 8

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 676

ttaacgtt 8

<210> 677

<211> 8

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 677

- 128 -

aaaacggtt

8

<210> 678  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 678

ataacggtt

8

<210> 679  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 679

aacgttct

8

<210> 680  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 680

tccgatcg

8

<210> 681  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 681

tccgtacg

8

<210> 682  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 682

gctagacgct agcgtga

17

<210> 683  
<211> 25  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 683  
gagaacgctg gacctcatca tccat 25

<210> 684  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 684  
gagaacgcta gaccttctat 20

<210> 685  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 685  
actagacgtt agtgtga 17

<210> 686  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 686  
cacaccttgg tcaatgtcac gt 22

<210> 687  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 687  
tctccatcct atggttttat cg 22

<210> 688  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 688  
cgctggacct tccat 15

- 130 -

<210> 689  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 689  
caccaccttg gtcaatgtca cgt 23

<210> 690  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 690  
gctagacgtt agctgga 17

<210> 691  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 691  
agtgcgattg cagatcg 17

<210> 692  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 692  
ttttcgtttt gtggttttgt ggtt 24

<210> 693  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 693  
ttttcgtttg tcgttttgtc gtt 23

<210> 694  
<211> 24  
<212> DNA  
<213> Artificial Sequence

- 131 -

<220>  
<223> Synthetic Sequence

<400> 694  
tttttgtttt gtggttttgt gggt 24

<210> 695  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 695  
accgcatgga ttctaggcca 20

<210> 696  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 696  
gctagacgtt agcgt 15

<210> 697  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 697  
aacgctggac cttccat 17

<210> 698  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (5)...(5)  
<223> m5c

<223> Synthetic Sequence

<400> 698  
tcaangtt 8

<210> 699  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

- 132 -

<400> 699  
ccttcgat 8

<210> 700  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 700  
actagacgtt agtgtga 17

<210> 701  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 701  
gctagaggtt agcgtga 17

<210> 702  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 702  
atggactctc cagcgttctc 20

<210> 703  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 703  
atcgactctc gagcgttctc 20

<210> 704  
<211> 13  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 704  
gctagacgtt agc 13

<210> 705  
<211> 9

- 133 -

<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 705  
gctagacgt 9  
  
<210> 706  
<211> 17  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 706  
agtgcgattc gagatcg 17  
  
<210> 707  
<211> 8  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<221> modified\_base  
<222> (5)...(5)  
<223> m5c  
  
<223> Synthetic Sequence  
  
<400> 707  
tcagngct 8  
  
<210> 708  
<211> 18  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 708  
ctgattgctc tctcgtga 18  
  
<210> 709  
<211> 8  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<221> modified\_base  
<222> (2)...(2)  
<223> m5c  
  
<223> Synthetic Sequence  
  
<400> 709  
tnaacgtt 8

- 134 -

<210> 710  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (6)...(6)  
<223> m5c

<223> Synthetic Sequence

<400> 710  
gagaangctg gaccttccat 20

<210> 711  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 711  
gctagacggtt aggctga 17

<210> 712  
<211> 14  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 712  
gctacttagc gtga 14

<210> 713  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 713  
gctaccttag cgtga 15

<210> 714  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 714  
atcgacttcg agcgttctc 19

<210> 715  
<211> 20



- 135 -

<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 715  
atgcactctg cagcgttctc 20

<210> 716  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 716  
agtgactctc cagcgttctc 20

<210> 717  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 717  
gccagatgtt agctgga 17

<210> 718  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 718  
atcgactoga gcgttctc 18

<210> 719  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 719  
atcgatcgag cgttctc 17

<210> 720  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> misc\_feature  
<222> (1)...(3)

- 136 -

<223> Conjugated to biotin moiety.

<223> Synthetic Sequence

<400> 720  
gagaacgctc gaccttcgat 20

<210> 721  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 721  
gctagacggt agctgga 17

<210> 722  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 722  
atcgactctc gagcgttctc 20

<210> 723  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 723  
tagacgttag cgtga 15

<210> 724  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 724  
cgactctcga gcgttctc 18

<210> 725  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 725  
ggggtcgacc ttggagggg g 21

<210> 726  
<211> 16  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 726  
gctaacgtta gcgtga 16

<210> 727  
<211> 9  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 727  
cgtcgctcgt 9

<210> 728  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (14)...(14)  
<223> m5c

<223> Synthetic Sequence

<400> 728  
gagaacgctg gacnttccat 20

<210> 729  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (18)...(18)  
<223> m5c

<223> Synthetic Sequence

<400> 729  
atcgacctac gtgcgttntc 20

<210> 730  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (3)...(3)

- 138 -

<223> m5c

<223> Synthetic Sequence

<400> 730  
atngacctac gtgcgttctc 20

<210> 731  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (7)...(7)  
<223> m5c

<223> Synthetic Sequence

<400> 731  
gctagangtt agcgt 15

<210> 732  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (14)...(14)  
<223> m5c

<223> Synthetic Sequence

<400> 732  
atcgactctc gagngttctc 20

<210> 733  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 733  
ggggtaatgc atcagggggg 20

<210> 734  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 734  
ggctgtattc ctgactgccc 20

<210> 735  
<211> 17

<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 735  
ccatgctaac ctctagc 17

<210> 736  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 736  
gctagatggt agcgtga 17

<210> 737  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 737  
cgtacottac ggtga 15

<210> 738  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 738  
tccatgctgg toctgatgct 20

<210> 739  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 739  
atcgactctc tcgagcgttc tc 22

<210> 740  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

- 140 -

<400> 740  
gctagagctt agcgtga 17

<210> 741  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 741  
atcgactctc gagtgttctc 20

<210> 742  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 742  
aacgctcgac cttcgat 17

<210> 743  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 743  
ctcaacgctg gaccttccat 20

<210> 744  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 744  
atcgacctac gtgcgttctc 20

<210> 745  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 745  
gagaatgctg gaccttccat 20

<210> 746  
<211> 17  
<212> DNA

- 141 -

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 746  
tcacgctaac ctctgac 17

<210> 747  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>

<221> misc\_feature  
<222> (1)...(3)  
<223> Conjugated to biotin moiety.

<223> Synthetic Sequence

<400> 747  
gagaacgctc cagcactgat 20

<210> 748  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>

<221> misc\_feature  
<222> (1)...(3)  
<223> Biotin moiety attached at 5' end of sequence.

<223> Synthetic Sequence

<400> 748  
gagcaagctg gaccttccat 20

<210> 749  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 749  
cgctagaggt tagcgtga 18

<210> 750  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 750  
gctagatggt aacgt 15

<210> 751

- 142 -

<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 751  
atggaaggtc cacgttctc 19

<210> 752  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 752  
gctagatggt agcgt 15

<210> 753  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 753  
gctagacggt agtgt 15

<210> 754  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 754  
tccatgacgg tcctgatgct 20

<210> 755  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 755  
tccatggcgg tcctgatgct 20

<210> 756  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence



- 143 -

<400> 756  
gctagacgat agcgt 15

<210> 757  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 757  
gctagtcgat agcgt 15

<210> 758  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 758  
tccatgacgt tcctgatgct 20

<210> 759  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 759  
tccatgtcgt tcctgatgct 20

<210> 760  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (13)...(13)  
<223> m5c

<223> Synthetic Sequence

<400> 760  
gctagacggt agngt 15

<210> 761  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 761

- 144 -

gctaggcggtt agcgt

15

<210> 762  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (8)...(8)  
<223> m5c

<223> Synthetic Sequence

<400> 762

tccatgtngg tcctgatgct

20

<210> 763  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (12)...(12)  
<223> m5c

<223> Synthetic Sequence

<400> 763

tccatgtcgg tncctgatgct

20

<210> 764  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<221> modified\_base  
<222> (3)...(3)  
<223> m5c

<221> modified\_base  
<222> (10)...(10)  
<223> m5c

<221> modified\_base  
<222> (14)...(14)  
<223> m5c

<400> 764

atngactctn gagngttctc

20

<210> 765  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>

- 145 -

<223> Synthetic Sequence

<400> 765  
atggaaggtc cagtgttctc 20

<210> 766  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 766  
gcatgacgtt gagct 15

<210> 767  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 767  
ggggtcaacg ttgagggggg 20

<210> 768  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 768  
ggggtcaagt ctgagggggg 20

<210> 769  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 769  
cgcgcgcgcg cgcgcgcgcg 20

<210> 770  
<211> 28  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 770  
cccccccccc ccccccccc cccccccc 28

<210> 771

- 146 -

<211> 35  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 771  
cccccccccc cccccccccc cccccccccc ccccc 35

<210> 772  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 772  
tccatgtcgc tcctgatcct 20

<210> 773  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 773  
gctaaacggt agcgt 15

<210> 774  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 774  
tccatgtcga tcctgatgct 20

<210> 775  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 775  
tccatgccgg tcctgatgct 20

<210> 776  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

- 147 -

<400> 776  
aaaatcaacg ttgaaaaaaa 20

<210> 777  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 777  
tccataacgt tcctgatgct 20

<210> 778  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 778  
tggaggtccc accgagatcg gag 23

<210> 779  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 779  
cgtcgtcgtc gtcgtcgtcg t 21

<210> 780  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 780  
ctgctgctgc tgctgctgct g 21

<210> 781  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 781  
gagaacgctc cgaccttcga t 21

<210> 782  
<211> 15

- 148 -

<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 782  
gctagatgtt agcgt 15

<210> 783  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 783  
gcatgacgtt gagct 15

<210> 784  
<211> 10  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> misc\_feature  
<222> (8)...(10)  
<223> Conjugated to FITC moiety.

<223> Synthetic Sequence

<400> 784  
tcaatgctga 10

<210> 785  
<211> 10  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> misc\_feature  
<222> (8)...(10)  
<223> Conjugated to FITC moiety.

<223> Synthetic Sequence

<400> 785  
tcaacgttga 10

<210> 786  
<211> 10  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> misc\_feature  
<222> (8)...(10)  
<223> Conjugated to biotin moiety.

<223> Synthetic Sequence

- 149 -

<400> 786  
tcaacgttga 10

<210> 787  
<211> 10  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> misc\_feature  
<222> (8)...(10)  
<223> Conjugated to biotin moiety.

<223> Synthetic Sequence

<400> 787  
gcaatattgc 10

<210> 788  
<211> 10  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> misc\_feature  
<222> (8)...(10)  
<223> Conjugated to FITC moiety.

<223> Synthetic Sequence

<400> 788  
gcaatattgc 10

<210> 789  
<211> 10  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 789  
agttgcaact 10

<210> 790  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 790  
tcttcgaa 8

<210> 791  
<211> 8  
<212> DNA  
<213> Artificial Sequence

- 150 -

<220>  
<223> Synthetic Sequence

<400> 791  
tcaacgctc 8

<210> 792  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 792  
ccatgtcggc cctgatgct 19

<210> 793  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 793  
gtttttatat aatttggg 18

<210> 794  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 794  
ttttttgttg tcgttttgtc gtt 23

<210> 795  
<211> 12  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 795  
ttgggggggg tt 12

<210> 796  
<211> 13  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 796  
gggggttggg gtt 13



- 151 -

<210> 797  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 797  
ggtggtgtag gttttgg 17

<210> 798  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> misc\_feature  
<222> (1)...(3)  
<223> Conjugated to biotin moiety.

<221> modified\_base  
<222> (6)...(6)  
<223> m5c

<223> Synthetic Sequence

<400> 798  
gagaangctc gaccttcgat 20

<210> 799  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 799  
tcaacgttaa cgtaaactt 20

<210> 800  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> misc\_feature  
<222> (1)...(3)  
<223> Conjugated to biotin moiety.

<221> modified\_base  
<222> (8)...(8)  
<223> m5c

<223> Synthetic Sequence

<400> 800  
gagcaagntg gaccttccat 20

<210> 801

- 152 -

<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<221> misc\_feature  
<222> (1)...(3)  
<223> Conjugated to biotin moiety.  
  
<221> modified\_base  
<222> (6)...(6)  
<223> m5c  
  
<223> Synthetic Sequence

<400> 801  
gagaangctc cagcactgat

20

<210> 802  
<211> 10  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<221> modified\_base  
<222> (5)...(5)  
<223> m5c  
  
<221> misc\_feature  
<222> (8)...(10)  
<223> Conjugated to biotin moiety.  
  
<223> Synthetic Sequence

<400> 802  
tcaangttga

10

<210> 803  
<211> 10  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<221> modified\_base  
<222> (2)...(2)  
<223> m5c  
  
<221> misc\_feature  
<222> (8)...(10)  
<223> Conjugated to biotin moiety.  
  
<223> Synthetic Sequence

<400> 803  
gnaatattgc

10

<210> 804  
<211> 24  
<212> DNA  
<213> Artificial Sequence

- 153 -

<220>  
<223> Synthetic Sequence

<400> 804  
tgctgctttt gtcgttttgt gctt 24

<210> 805  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 805  
ctgcgttagc aatttaactg tg 22

<210> 806  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 806  
tccatgacgt tcttgatgct 20

<210> 807  
<211> 28  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 807  
tgcattgccgt gcatccgtac acagctct 28

<210> 808  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 808  
tgcattgccgt acacagctct 20

<210> 809  
<211> 12  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 809  
tgcattcagct ct 12

- 154 -

<210> 810  
<211> 8  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 810  
tgcgctct 8  
  
<210> 811  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 811  
cccccccccc ccccccccc 20  
  
<210> 812  
<211> 12  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 812  
cccccccccc cc 12  
  
<210> 813  
<211> 8  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 813  
cccccccc 8  
  
<210> 814  
<211> 12  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 814  
tgcacagct ct 12  
  
<210> 815  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>

- 155 -

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 815

tgcatgccgt acacagctct

20

&lt;210&gt; 816

&lt;211&gt; 20

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 816

gagcaagctg gaccttccat

20

&lt;210&gt; 817

&lt;211&gt; 32

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 817

tcaacgttaa cgttaacgtt aacgttaacg tt

32

&lt;210&gt; 818

&lt;211&gt; 20

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 818

gagaacgctc gaccttcgat

20

&lt;210&gt; 819

&lt;211&gt; 25

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 819

gtccccattt cccagaggag gaaat

25

&lt;210&gt; 820

&lt;211&gt; 25

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 820

ctagcggctg acgtcatcaa gctag

25

&lt;210&gt; 821

- 156 -

<211> 25  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 821  
ctagcttgat gacgtcagcc gctag 25

<210> 822  
<211> 16  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 822  
cggtcgacgt catcaa 16

<210> 823  
<211> 8  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 823  
ctgacgtg 8

<210> 824  
<211> 10  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 824  
ctgacgtcat 10

<210> 825  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 825  
attcgatcgg ggcggggcga g 21

<210> 826  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

- 157 -

<400> 826  
ctcgccccgc cccgatcgaa t 21

<210> 827  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 827  
gactgacgtc agcgt 15

<210> 828  
<211> 26  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 828  
ctagcggctg acgtcataaa gctagc 26

<210> 829  
<211> 26  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 829  
ctagctttat gacgtcagcc gctagc 26

<210> 830  
<211> 26  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 830  
ctagcggctg agctcataaa gctagc 26

<210> 831  
<211> 25  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 831  
ctagtggctg acgtcatcaa gctag 25

<210> 832  
<211> 20

- 158 -

<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 832  
tccaccacgt ggtctatgct 20

<210> 833  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 833  
gggaatgaaa gattttatta taag 24

<210> 834  
<211> 26  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 834  
tctaaaaacc atctattctt aaccct 26

<210> 835  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 835  
agctcaacgt catgc 15

<210> 836  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 836  
ttaacggtgg tagcgtatt ggtc 24

<210> 837  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence



- 159 -

<400> 837  
ttaagaccaa taccgtacc accg 24

<210> 838  
<211> 25  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 838  
gatctagtga tgagtcagcc ggatc 25

<210> 839  
<211> 25  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 839  
gatccggctg actcatcact agatc 25

<210> 840  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 840  
tccaagacgt tcctgatgct 20

<210> 841  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 841  
tccatgacgt ccctgatgct 20

<210> 842  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 842  
tccaccacgt ggctgatgct 20

<210> 843  
<211> 17  
<212> DNA

- 160 -

<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 843  
ccacgtggac ctctagc 17

<210> 844  
<211> 27  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 844  
tcagaccacg tggtcgggtg ttctga 27

<210> 845  
<211> 27  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 845  
tcaggaacac ccgaccacgt ggtctga 27

<210> 846  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 846  
catttcacg atttccca 18

<210> 847  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 847  
ttcctctctg caagagact 19

<210> 848  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 848

- 161 -

tgtatctctc tgaaggact

19

<210> 849  
<211> 25  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 849  
ataaagcgaa actagcagca gtttc

25

<210> 850  
<211> 25  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 850  
gaaactgctg ctagtttcgc tttat

25

<210> 851  
<211> 30  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 851  
tgcccaaaga ggaaaatttg tttcatacag

30

<210> 852  
<211> 30  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 852  
ctgtatgaaa caaattttcc tctttgggca

30

<210> 853  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 853  
ttagggtag ggtagggtt

20

<210> 854  
<211> 20  
<212> DNA  
<213> Artificial Sequence

- 162 -

<220>  
<223> Synthetic Sequence

<400> 854  
tccatgagct tcctgatgct 20

<210> 855  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 855  
aaaacatgac gttcaaaaaa 20

<210> 856  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 856  
aaaacatgac gttcgggggg 20

<210> 857  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 857  
ggggcatgag cttcgggggg 20

<210> 858  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 858  
ctaggctgac gtcacaaagc tagt 24

<210> 859  
<211> 30  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 859  
tctgacgtca tctgacgttg gctgacgtct 30

- 163 -

<210> 860  
<211> 25  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 860  
ggaattagta atagatatag aagtt 25

<210> 861  
<211> 30  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 861  
tttacctttt ataaacataa ctaaaacaaa 30

<210> 862  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 862  
gcgttttttt ttgcg 15

<210> 863  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 863  
atatctaatac aaaacattaa caaa 24

<210> 864  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 864  
tctatcccag gtggttcctg ttag 24

<210> 865  
<211> 20  
<212> DNA  
<213> Artificial Sequence

- 164 -

<220>  
<221> misc\_feature  
<222> (1)...(3)  
<223> Conjugated to biotin moiety.  
  
<223> Synthetic Sequence  
  
<400> 865  
tccatgacgt tcctgatgct 20  
  
<210> 866  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<221> misc\_feature  
<222> (1)...(3)  
<223> Conjugated to biotin moiety.  
  
<223> Synthetic Sequence  
  
<400> 866  
tccatgagct tcctgatgct 20  
  
<210> 867  
<211> 13  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<221> misc\_feature  
<222> (11)...(13)  
<223> Conjugated to FITC moiety.  
  
<221> misc\_feature  
<222> (0)...(0)  
<223> Has phosphodiester backbone.  
  
<223> Synthetic Sequence  
  
<400> 867  
tttttttttt ttt 13  
  
<210> 868  
<211> 13  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<221> misc\_feature  
<222> (11)...(13)  
<223> Conjugated to biotin moiety.  
  
<221> misc\_feature  
<222> (0)...(0)  
<223> Has phosphorothioate and phosphodiester chimeric backbone with phosphodiester on 3' end.  
  
<223> Synthetic Sequence

- 165 -

<400> 868  
tttttttttt ttt 13

<210> 869  
<211> 25  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 869  
ctagcttgat gagctcagcc gctag 25

<210> 870  
<211> 25  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 870  
ttcagttgct ttgctgctta gctaa 25

<210> 871  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 871  
tccatgagct tcctgagtct 20

<210> 872  
<211> 25  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 872  
ctagcggctg acgtcatcaa tctag 25

<210> 873  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 873  
tgctagctgt gcctgtacct 20

<210> 874  
<211> 23  
<212> DNA

- 166 -

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 874  
atgctaaagg acgtcacatt gca 23

<210> 875  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 875  
tgcaatgtga cgtccttttag cat 23

<210> 876  
<211> 31  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 876  
gtaggggact ttccgagctc gagatcctat g 31

<210> 877  
<211> 31  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 877  
cataggatct cgagctcgga aagtccccta c 31

<210> 878  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 878  
ctgtcaggaa ctgcaggtaa gg 22

<210> 879  
<211> 27  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 879



- 167 -  
27

cataacatag gaatattttac tcctcgc

<210> 880  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 880

ctccagctcc aagaaaggac g

21

<210> 881  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 881

gaagtttctg gtaagtcttc g

21

<210> 882  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 882

tgctgctttt gtgcttttgt gctt

24

<210> 883  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 883

tcgtcgtttt gtggttttgt gggt

24

<210> 884  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 884

tcgtcgtttg tcgttttgc gtt

23

<210> 885  
<211> 22  
<212> DNA  
<213> Artificial Sequence

- 168 -

<220>  
<223> Synthetic Sequence

<400> 885  
tcctgacgtt cggcgcgcgc cc 22

<210> 886  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 886  
tgctgctttt gtgcttttgt gctt 24

<210> 887  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 887  
tccatgagct tcctgagctt 20

<210> 888  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 888  
tcgtcgtttc gtcgttttga cggt 24

<210> 889  
<211> 26  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 889  
tcgtcgtttg cgtgcgtttc gtcgtt 26

<210> 890  
<211> 27  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 890  
tcgcgtgcgt tttgtcgttt tgacgtt 27

- 169 -

<210> 891  
<211> 25  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 891  
ttcgtcgtttt tgtcgttttg tcggt 25  
  
<210> 892  
<211> 15  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 892  
tcctgacggg gaagt 15  
  
<210> 893  
<211> 15  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 893  
tcctggcgtg gaagt 15  
  
<210> 894  
<211> 15  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 894  
tcctggcggg gaagt 15  
  
<210> 895  
<211> 15  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 895  
tcctggcggtt gaagt 15  
  
<210> 896  
<211> 15  
<212> DNA  
<213> Artificial Sequence

- 170 -

<220>  
<223> Synthetic Sequence

<400> 896  
tcctgacgtg gaagt 15

<210> 897  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 897  
gcgacgttcg gcgcgcgccc 20

<210> 898  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 898  
gcgacgggcg gcgcgcgccc 20

<210> 899  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 899  
gcggcggtcg gcgcgcgccc 20

<210> 900  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 900  
gcggcggtcg gcgcgcgccc 20

<210> 901  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 901  
gcgacgggtcg gcgcgcgccc 20

- 171 -

<210> 902  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 902  
gcggcggttcg gcgcgcgccc 20  
  
<210> 903  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 903  
gcgacgtgcg gcgcgcgccc 20  
  
<210> 904  
<211> 15  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 904  
tcgtcgctgt ctccg 15  
  
<210> 905  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 905  
tgtgggggtt ttggtttttg 20  
  
<210> 906  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 906  
aggggagggg aggggagggg 20  
  
<210> 907  
<211> 21  
<212> DNA  
<213> Artificial Sequence  
  
<220>

- 172 -

<223> Synthetic Sequence

<400> 907  
tgtgtgtgtg tgtgtgtgtg t 21

<210> 908  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 908  
ctctctctct ctctctctct ct 22

<210> 909  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 909  
ggggtcgacg tcgagggggg 20

<210> 910  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 910  
atatatatat atatatatat at 22

<210> 911  
<211> 27  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 911  
tttttttttt tttttttttt ttttttt 27

<210> 912  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 912  
tttttttttt tttttttttt t 21

<210> 913

- 173 -

<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 913  
tttttttttt tttttttt 18

<210> 914  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 914  
gctagagggg aggggt 15

<210> 915  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 915  
gctagatgtt agggg 15

<210> 916  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 916  
gcatgagggg gagct 15

<210> 917  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 917  
atggaaggtc cagggggctc 20

<210> 918  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

- 174 -

<400> 918  
atggactctg gagggggctc 20

<210> 919  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 919  
atggaaggtc caaggggctc 20

<210> 920  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 920  
gagaaggggg gaccttgat 20

<210> 921  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 921  
gagaaggggg gaccttccat 20

<210> 922  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 922  
gagaaggggc cagcactgat 20

<210> 923  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 923  
tccatgtggg gcctgatgct 20

<210> 924  
<211> 20



- 175 -

<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 924  
tccatgaggg gcctgatgct 20

<210> 925  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 925  
tccatgtggg gcctgctgat 20

<210> 926  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 926  
atggactctc cggggttctc 20

<210> 927  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 927  
atggaaggtc cggggttctc 20

<210> 928  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 928  
atggactctg gaggggtctc 20

<210> 929  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

- 176 -

<400> 929  
atggaggctc catggggctc 20

<210> 930  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 930  
atggactctg gggggttctc 20

<210> 931  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 931  
tccatgtggg tggggatgct 20

<210> 932  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 932  
tccatgcggg tggggatgct 20

<210> 933  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 933  
tccatggggg tcctgatgct 20

<210> 934  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 934  
tccatggggg ccctgatgct 20

<210> 935  
<211> 20  
<212> DNA

- 177 -

<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 935  
tccatggggt gcctgatgct 20

<210> 936  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 936  
tccatggggt tcctgatgct 20

<210> 937  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 937  
tccatcgggg gcctgatgct 20

<210> 938  
<211> 14  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 938  
gctagaggga gtgt 14

<210> 939  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Synthetic Sequence

<400> 939  
tttttttttt tttttttt 18

<210> 940  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>

<221> misc\_difference  
<222> (2)...(2)  
<223> m is a or c

- 178 -

<221> misc\_difference  
<222> (18)...(18)  
<223> m i s a o r c  
  
<223> Synthetic Sequence  
  
<400> 940  
gmgtcaacg ttgagggm g 21  
  
<210> 941  
<211> 21  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 941  
gggagttcg ttgaggggg g 21  
  
<210> 942  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 942  
tcgtcgtttc ccccccccc 20  
  
<210> 943  
<211> 25  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 943  
ttggggggtt ttttttttt tttt 25  
  
<210> 944  
<211> 23  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 944  
tttaaatttt aaaatttaa ata 23  
  
<210> 945  
<211> 24  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence

- 179 -

<400> 945  
ttgggtttttt tgggtttttt ttgg 24

<210> 946  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 946  
tttccctttt ccccttttcc cctc 24

<210> 947  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> misc\_difference  
<222> (21)...(21)  
<223> s is g or c

<223> Synthetic Sequence

<400> 947  
ggggtcacgc atgagggggg s 21

<210> 948  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 948  
tccatgacgt tcctgacgtt 20

<210> 949  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 949  
tccatgacgt tcctgacgtt 20

<210> 950  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 950

- 180 -

tccatgacgt tcctgacgtt 20

<210> 951  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 951  
tccatgacgt tcctgacgtt 20

<210> 952  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 952  
tccatgacgt tcctgacgtt 20

<210> 953  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 953  
tccatgacgt tcctgacgtt 20

<210> 954  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 954  
tccatgacgt tcctgacgtt 20

<210> 955  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 955  
tccatgacgt tcctgacgtt 20

<210> 956  
<211> 20  
<212> DNA  
<213> Artificial Sequence

- 181 -

<220>  
<223> Synthetic Sequence

<400> 956  
tccatgacgt tcctgacgtt 20

<210> 957  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 957  
tccatgacgt tcctgacgtt 20

<210> 958  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 958  
tccatgacgt tcctgacgtt 20

<210> 959  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 959  
gggggacgat cgtcggggg 19

<210> 960  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 960  
gggggtcgta cgacggggg 20

<210> 961  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 961  
tttttttttt tttttttttt tttt 24

- 182 -

<210> 962  
<211> 24  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 962  
aaaaaaaaaa aaaaaaaaaa aaaa 24  
  
<210> 963  
<211> 24  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 963  
cccccccccc ccccccccc cccc 24  
  
<210> 964  
<211> 24  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 964  
tcgtcgtttt gtcgttttgc cgtt 24  
  
<210> 965  
<211> 24  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 965  
tcgtcgtttt gtcgttttgc cgtt 24  
  
<210> 966  
<211> 24  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 966  
tcgtcgtttt gtcgttttgc cgtt 24  
  
<210> 967  
<211> 24  
<212> DNA  
<213> Artificial Sequence



- 183 -

<220>  
<223> Synthetic Sequence

<400> 967  
tcgtcgtttt gtcgttttgt cgtt 24

<210> 968  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 968  
ggggtcaacg ttgagggggg 20

<210> 969  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 969  
ggggtcaacg ttgagggggg 20

<210> 970  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 970  
ggggtcaagc ttgagggggg 20

<210> 971  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 971  
tgctgcttcc ccccccccc 20

<210> 972  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 972  
ggggacgtcg acgtggggg 20

- 184 -

<210> 973  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 973  
gggggtcgtcg acgagggggg 20

<210> 974  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 974  
gggggtcgacg tacgtcgagg gggg 24

<210> 975  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 975  
ggggaccggt accggtgggg gg 22

<210> 976  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 976  
gggtcgacgt cgagggggg 19

<210> 977  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 977  
gggggtcgacg tcgaggggg 19

<210> 978  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>

- 185 -

<223> Synthetic Sequence

<400> 978  
ggggaacggtt aacgttgggg gg 22

<210> 979  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 979  
ggggtcaccg gtgagggggg 20

<210> 980  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 980  
ggggtcggttc gaacgagggg gg 22

<210> 981  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 981  
ggggacgttc gaacgtgggg gg 22

<210> 982  
<211> 10  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 982  
tcaactttga 10

<210> 983  
<211> 10  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 983  
tcaagcttga 10

<210> 984

- 186 -

<211> 12  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 984  
tcacgatcgt ga 12  
  
<210> 985  
<211> 12  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 985  
tcagcatgct ga 12  
  
<210> 986  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 986  
gggggagcat gctggggggg 20  
  
<210> 987  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 987  
gggggggggg gggggggggg 20  
  
<210> 988  
<211> 22  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 988  
gggggacgat atcgtcggg gg 22  
  
<210> 989  
<211> 22  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence

- 187 -

<400> 989  
gggggacgac gtcgtcgggg gg 22  
  
<210> 990  
<211> 22  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 990  
gggggacgag ctcgtcgggg gg 22  
  
<210> 991  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 991  
gggggacgta cgtcgggggg 20  
  
<210> 992  
<211> 8  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 992  
tcaacggt 8  
  
<210> 993  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 993  
tccataccgg tcctgatgct 20  
  
<210> 994  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 994  
tccataccgg tcctaccggt 20  
  
<210> 995  
<211> 20

- 188 -

<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 995  
gggggacgat cggtgggggg 20

<210> 996  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 996  
ggggaacgat cgtcgggggg 20

<210> 997  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 997  
ggggggacga tcgtcggggg g 21

<210> 998  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 998  
gggggacgat cgtcgggggg g 21

<210> 999  
<211> 12  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 999  
aaagacgtta aa 12

<210> 1000  
<211> 12  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1000  
aaagagctta aa 12

<210> 1001  
<211> 12  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (6)...(6)  
<223> m5c

<223> Synthetic Sequence

<400> 1001  
aaagangtta aa 12

<210> 1002  
<211> 12  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1002  
aaattcggaa aa 12

<210> 1003  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1003  
gggggtcatc gatgaggggg g 21

<210> 1004  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1004  
gggggtcaac gttgaggggg g 21

<210> 1005  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1005  
atgtagctta ataacaagc 20

- 190 -

<210> 1006  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1006  
ggatcccttg agttacttct 20

<210> 1007  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1007  
ccattccact tctgattacc 20

<210> 1008  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1008  
tatgtattat catgtagata 20

<210> 1009  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1009  
agcctacgta ttcaccctcc 20

<210> 1010  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1010  
ttcctgcaac tactattgta 20

<210> 1011  
<211> 20  
<212> DNA  
<213> Artificial Sequence



- 191 -

<220>  
<223> Synthetic Sequence

<400> 1011  
atagaaggcc ctacaccagt 20

<210> 1012  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1012  
ttacaccggt ctatggaggt 20

<210> 1013  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1013  
ctaaccagat caagtctagg 20

<210> 1014  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1014  
cctagacttg atctggttag 20

<210> 1015  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1015  
tataagcctc gtccgacatg 20

<210> 1016  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1016  
catgtcggac gaggcttata 20

- 192 -

<210> 1017  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 1017  
tgggtggtggg gagtaagctc 20  
  
<210> 1018  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 1018  
gagctactcc cccaccacca 20  
  
<210> 1019  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 1019  
gccttcgatc ttcggttgga 20  
  
<210> 1020  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 1020  
tggacttctc ttgcccgtct 20  
  
<210> 1021  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 1021  
atgctgtagc ccagcgataa 20  
  
<210> 1022  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>

- 193 -

<223> Synthetic Sequence

<400> 1022  
accgaatcag cggaagtga 20

<210> 1023  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1023  
tccatgacgt tctgacgtt 20

<210> 1024  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1024  
ggagaaacc atgagctcat ctgg 24

<210> 1025  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1025  
accacagacc agcaggcaga 20

<210> 1026  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1026  
gagcgtgaac tgcgcgaaga 20

<210> 1027  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1027  
tcggtaccct tgcagcggtt 20

<210> 1028

- 194 -

<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1028  
ctggagccct agccaaggat 20

<210> 1029  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1029  
gcgactccat caccagcgat 20

<210> 1030  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1030  
cctgaagtaa gaaccagatg t 21

<210> 1031  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1031  
ctgtgttatc tgacatacac c 21

<210> 1032  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1032  
aattagcctt aggtgattgg g 21

<210> 1033  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

- 195 -

<400> 1033  
acatctggtt cttacttcag g 21

<210> 1034  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1034  
ataagtcata ttttggaac tac 23

<210> 1035  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1035  
cccaatcacc taaggcta t 21

<210> 1036  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1036  
ggggtcgtcg acgagggggg 20

<210> 1037  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1037  
ggggtcgttc gaacgagggg gg 22

<210> 1038  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1038  
ggggacgttc gaacgtggg gg 22

<210> 1039  
<211> 15

- 196 -

<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified base  
<222> (9)...(9)  
<223> n is 5-methylcytosine.

<223> Synthetic Sequence

<400> 1039  
tcctggcgng gaagt 15

<210> 1040  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1040  
ggggaacgac gtcgttgggg gg 22

<210> 1041  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1041  
ggggaacgta cgtcgggggg 20

<210> 1042  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1042  
ggggaacgta cgtacgttgg gggg 24

<210> 1043  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1043  
ggggtcaccg gtgagggggg 20

<210> 1044  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1044  
ggggtcgacg tacgtcgagg gggg 24

<210> 1045  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1045  
ggggaccggt accggtgggg gg 22

<210> 1046  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1046  
gggtcgacgt cgagggggg 19

<210> 1047  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1047  
ggggtcgacg tcgagggg 18

<210> 1048  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1048  
ggggaacggt aacgttgggg gg 22

<210> 1049  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1049  
ggggacgtcg acgtggggg 19

- 198 -

<210> 1050  
<211> 34  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1050  
gcactcttgc aagctacagc cggcagcctc tgat 34

<210> 1051  
<211> 32  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1051  
cggctcttcc atgaggtctt tgctaattctt gg 32

<210> 1052  
<211> 35  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1052  
cggctcttcc atgaaagtct ttggacgatg tgagc 35

<210> 1053  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1053  
tcctgcaggc taagt 15

<210> 1054  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1054  
gggggtcggt cgttgggggg 20

<210> 1055  
<211> 20  
<212> DNA  
<213> Artificial Sequence



- 199 -

<220>  
<223> Synthetic Sequence

<400> 1055  
gggggatgat tggtgggggg 20

<210> 1056  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> modified\_base  
<222> (7)...(7)  
<223> m5c

<221> modified\_base  
<222> (11)...(11)  
<223> m5c

<223> Synthetic Sequence

<400> 1056  
gggggangat nggtgggggg 20

<210> 1057  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1057  
gggggagcta gcttgggggg 20

<210> 1058  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1058  
ggttcttttg gtccttgtct 20

<210> 1059  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1059  
ggttcttttg gtcctcgtct 20

<210> 1060  
<211> 20  
<212> DNA

- 200 -

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 1060

ggttcttttg gtccttatct

20

&lt;210&gt; 1061

&lt;211&gt; 20

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 1061

ggttcttggg ttccttgtct

20

&lt;210&gt; 1062

&lt;211&gt; 20

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 1062

tggtcttttg gtccttgtct

20

&lt;210&gt; 1063

&lt;211&gt; 20

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 1063

ggttcaaag gtccttgtct

20

&lt;210&gt; 1064

&lt;211&gt; 20

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 1064

gggtcttttg ggccttgtct

20

&lt;210&gt; 1065

&lt;211&gt; 24

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Sequence

&lt;400&gt; 1065

- 201 -

tccaggactt ctctcaggtt tttt

24

<210> 1066  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 1066

tccaaaactt ctctcaaatt

20

<210> 1067  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 1067

tactactttt atacttttat actt

24

<210> 1068  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 1068

tgtgtgtgtg tgtgtgtgtg tgtg

24

<210> 1069  
<211> 25  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 1069

ttgttgttgt tgtttgttgt tgttg

25

<210> 1070  
<211> 27  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

&lt;400&gt; 1070

ggctccgggg aggggaatttt tgtctat

27

<210> 1071  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1071  
gggacgatcg tcggggggg 19

<210> 1072  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1072  
gggtcgtcga cgaggggggg 20

<210> 1073  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1073  
ggtcgtcgac gaggggggg 19

<210> 1074  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1074  
gggtcgtcgt cgtggggggg 20

<210> 1075  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1075  
ggggacgatc gtcggggggg 20

<210> 1076  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1076  
ggggacgtcg tcgtgggggg 20

<210> 1077  
<211> 27  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1077  
ggggtcgacg tcgacgtcga gggggggg 27

<210> 1078  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1078  
ggggaaccgc ggttgggggg g 21

<210> 1079  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1079  
ggggacgacg tcgtgggggg g 21

<210> 1080  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1080  
tcgtcgtcgt cgtcgtgggg ggg 23

<210> 1081  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1081  
tcctgccggg gaagt 15

<210> 1082  
<211> 15  
<212> DNA  
<213> Artificial Sequence

- 204 -

<220>  
<223> Synthetic Sequence

<400> 1082  
tcctgcaggg gaagt 15

<210> 1083  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1083  
tcctgaaggg gaagt 15

<210> 1084  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1084  
tcctggcggg caagt 15

<210> 1085  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1085  
tcctggcggg taagt 15

<210> 1086  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1086  
tcctggcggg aaagt 15

<210> 1087  
<211> 15  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Synthetic Sequence

<400> 1087  
tccgggcggg gaagt 15

- 205 -

<210> 1088  
<211> 15  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 1088  
tcggggcgagg gaagt 15  
  
<210> 1089  
<211> 15  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 1089  
tcccgaggcgagg gaagt 15  
  
<210> 1090  
<211> 15  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 1090  
gggggacggtt ggggg 15  
  
<210> 1091  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 1091  
gggggtttttt ttttgggggg 20  
  
<210> 1092  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Synthetic Sequence  
  
<400> 1092  
ggggccccc ccccgggggg 20  
  
<210> 1093  
<211> 21  
<212> DNA  
<213> Artificial Sequence  
  
<220>

- 206 -

<223> Synthetic Sequence

<400> 1093

ggggttggtg ttggtggggg g

21



**This Page is Inserted by IFW Indexing and Scanning  
Operations and is not part of the Official Record**

**BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☒ **BLACK BORDERS**
- ☐ **IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- ☐ **FADED TEXT OR DRAWING**
- ☐ **BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- ☐ **SKEWED/SLANTED IMAGES**
- ☐ **COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- ☐ **GRAY SCALE DOCUMENTS**
- ☐ **LINES OR MARKS ON ORIGINAL DOCUMENT**
- ☐ **REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- ☐ **OTHER:** \_\_\_\_\_

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.**